WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent	ternational Patent Classification 6:		(1	1) International Publication Number:	WO 99/31236	
C12N 15/12, C07 1/68	K 14/47, 16/18, C12Q	A2	(4	3) International Publication Date:	24 June 1999 (24.06.99)	
(21) International Applica (22) International Filing 1 (30) Priority Data: 60/069,957 60/074,121 60/081,563 60/096,116 (71) Applicant (for all de [FR/FR]; 24, rue R (72) Inventors; and (75) Inventors/Applicants die [FR/FR]; 108, (FR). DUCLERT, F-94100 Saint-Me Jean-Baptiste [FR/Paris (FR). (74) Agents: MARTIN, Je		GENSI RET, I O Vanv Victori WARI , F-750	US US US US US US US US OS,	(81) Designated States: AL, AM, AT, BY, CA, CH, CN, CU, CZ, DE GH, GM, HR, HU, ID, IL, IN, KZ, LC, LK, LR, LS, LT, LU MW, MX, NO, NZ, PL, PT, RC SL, TJ, TM, TR, TT, UA, UC ARIPO patent (GH, GM, KE, L Eurasian patent (AM, AZ, BY, L European patent (AT, BE, CH, GB, GR, IE, IT, LU, MC, NL, BJ, CF, CG, CI, CM, GA, GN TD, TG). Published Without international search re upon receipt of that report.	i, DK, EE, ES, FI, GB, GE, IS, JP, KE, KG, KP, KR, LV, MD, MG, MK, MN, D, RU, SD, SE, SG, SI, SK, G, US, UZ, VN, YU, ZW, S, MW, SD, SZ, UG, ZW) KG, KZ, MD, RU, TJ, TM) CY, DE, DK, ES, FI, FR PT, SE), OAPI patent (BF, GW, ML, MR, NE, SN	
TO DOLL THE HOLL						
	DNAs FOR SECRETED PRO	TEINS				

(57) Abstract

The sequences of extended cDNAs encoding secreted proteins are disclosed. The extended cDNAs can be used to express secreted proteins or portions thereof or to obtain antibodies capable of specifically binding to the secreted proteins. The extended cDNAs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. The extended cDNAs may also be used to design expression vectors and secretion vectors.

A9

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	Sl	Slovenia
AM	Armenia	FI	Pinland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	Prance	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TC	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
8G	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	E	Ireland	MN	Mongoira	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauntania	UG	Uganda
BY	Belarus	IS	(celand	.MW	Malawi	US	United States of America
CA	Canada	iT	Italy	МX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	٧N	Viet Nam
CG	Congo	KE	Келуа	NI.	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwc
CI	Côte d'Ivoire	KP	Democratic People's	٧Z	Yew Zealand		
CM	Cameroon		Republic of Korea	PL	Proland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	ко	Romania		
cz	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	, SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

WO 99/31236 PCT/IB98/02122

EXTENDED cDNAS for secreted proteins

The present application relates to extended cDNAs which were disclosed in several United States Provisional Patent Applications. Table I lists the SEQ ID Nos. of the extended cDNAs in the present application, the SEQ ID Nos. of the identical or nearly identical extended cDNAs in the provisional applications, and the identities of the provisional applications in which the extended cDNAs were disclosed.

Background of the Invention

The estimated 50,000-100,000 genes scattered along the human chromosomes offer tremendous promise for the understanding, diagnosis, and treatment of human diseases. In addition, probes capable of specifically hybridizing to loci distributed throughout the human genome find applications in the construction of high resolution chromosome maps and in the identification of individuals.

In the past, the characterization of even a single human gene was a painstaking process, requiring years of effort. Recent developments in the areas of cloning vectors, DNA sequencing, and computer technology have merged to greatly accelerate the rate at which human genes can be isolated, sequenced, mapped, and characterized. Cloning vectors such as yeast artificial chromosomes (YACs) and bacterial artificial chromosomes (BACs) are able to accept DNA inserts ranging from 300 to 1000 kilobases (kb) or 100-400 kb in length respectively, thereby facilitating the manipulation and ordering of DNA sequences distributed over great distances on the human chromosomes. Automated DNA sequencing machines permit the rapid sequencing of human genes. Bioinformatics software enables the comparison of nucleic acidiand protein sequences, thereby assisting in the characterization of human gene products.

Currently, two different approaches are being pursued for identifying and characterizing the genes distributed along the human genome. In one approach, large fragments of genomic DNA are isolated, cloned, and sequenced. Potential open reading frames in these genomic sequences are identified using bio-informatics software. However, this approach entails sequencing large stretches of human DNA which do not encode proteins in order to find the protein encoding sequences scattered throughout the genome. In addition to requiring extensive sequencing, the bio-informatics software may mischaracterize the genomic sequences obtained. Thus, the software may produce false positives in which non-coding DNA is mischaracterized as coding DNA or false negatives in which coding DNA is mischaracterized as non-coding DNA.

An alternative approach takes a more direct route to identifying and characterizing human genes. In this approach, complementary DNAs (cDNAs) are synthesized from isolated messenger RNAs (mRNAs) which encode human proteins. Using this approach, sequencing is only performed on DNA which is derived from protein coding portions of the genome. Often, only short stretches of the cDNAs are sequenced to obtain sequences called expressed sequence tags (ESTs). The ESTs may then be used to isolate or purify extended cDNAs which include sequences adjacent to the EST sequences. The extended cDNAs may contain all of the sequence of the EST which was used to obtain them or only a portion of the sequence of the EST which was used to obtain them. In addition, the extended cDNAs may contain the full coding sequence of the gene from which the EST was derived or, alternatively, the extended cDNAs may include

WO 99/31236

15

portions of the coding sequence of the gene from which the EST was derived. It will be appreciated that there may be several extended cDNAs which include the EST sequence as a result of alternate splicing or the activity of alternative promoters.

In the past, the short EST sequences which could be used to isolate or purify extended cDNAs were often 5 obtained from oligo-dT primed cDNA libraries. Accordingly, they mainly corresponded to the 3' untranslated region of the mRNA. In part, the prevalence of EST sequences derived from the 3' end of the mRNA is a result of the fact that typical techniques for obtaining cDNAs, are not well suited for isolating cDNA sequences derived from the 5' ends of mRNAs. (Adams et al., Nature 377:174, 1996, Hillier et al., Genome Res. 6:807-828, 1996).

In addition, in those reported instances where longer cDNA sequences have been obtained, the reported 10 sequences typically correspond to coding sequences and do not include the full 5' untranslated region of the mRNA from which the cDNA is derived. Such incomplete sequences may not include the first exon of the mRNA, particularly in situations where the first exon is short. Furthermore, they may not include some exons, often short ones, which are located upstream of splicing sites. Thus, there is a need to obtain sequences derived from the 5' ends of mRNAs which can be used to obtain extended cDNAs which may include the 5' sequences contained in the 5' ESTs.

While many sequences derived from human chromosomes have practical applications, approaches based on the identification and characterization of those chromosomal sequences which encode a protein product are particularly relevant to diagnostic and therapeutic uses. Of the 50,000-100,000 protein coding genes, those genes encoding proteins which are secreted from the cell in which they are synthesized, as well as the secreted proteins themselves, are particularly valuable as potential therapeutic agents. Such proteins are often involved in cell to cell communication and 20 may be responsible for producing a clinically relevant response in their target cells.

In fact, several secretory proteins, including tissue plasminogen activator, G-CSF, GM-CSF, erythropoietin, human growth hormone, insulin, interferon-α, interferon-β, interferon-y, and interleukin-2, are currently in clinical use. These proteins are used to treat a wide range of conditions, including acute myocardial infarction, acute ischemic stroke, anemia, diabetes, growth hormone deficiency, hepatitis, kidney carcinoma, chemotherapy induced neutropenia and 25 multiple sclerosis. For these reasons, extended cDNAs encoding secreted proteins or portions thereof represent a particularly valuable source of therapeutic agents. Thus, there is a need for the identification and characterization of secreted proteins and the nucleic acids encoding them.

in addition to being therapeutically useful themselves, secretory proteins include short peptides, called signal peptides, at their amino termini which direct their secretion. These signal peptides are encoded by the signal sequences 30 located at the 5' ends of the coding sequences of genes encoding secreted proteins. Because these signal peptides will direct the extracellular secretion of any protein to which they are operably linked, the signal sequences may be exploited to direct the efficient secretion of any protein by operably linking the signal sequences to a gene encoding the protein for which secretion is desired. This may prove beneficial in gene therapy strategies in which it is desired to deliver a particular gene product to cells other than the cell in which it is produced. Signal sequences encoding signal peptides

also find application in simplifying protein purification techniques. In such applications, the extracellular secretion of the desired protein greatly facilitates purification by reducing the number of undesired proteins from which the desired protein must be selected. Thus, there exists a need to identify and characterize the 5' portions of the genes for secretory proteins which encode signal pentides.

Public information on the number of human genes for which the promoters and upstream regulatory regions have been identified and characterized is quite limited. In part, this may be due to the difficulty of isolating such regulatory sequences. Upstream regulatory sequences such as transcription factor binding sites are typically too short to be utilized as probes for isolating promoters from human genomic libraries. Recently, some approaches have been developed to isolate human promoters. One of them consists of making a CpG island library (Cross, S.H. et al., 10 Purification of CpG Islands using a Methylated DNA Binding Column, Nature Genetics 6: 236-244 (1994)). The second consists of isolating human genomic DNA sequences containing Spel binding sites by the use of Spel binding protein. (Mortlock et al., Genome Res. 6:327-335, 1996). Both of these approaches have their limits due to a lack of specificity or of comprehensiveness.

5' ESTs and extended cDNAs obtainable therefrom may be used to efficiently identify and isolate upstream 15 regulatory regions which control the location, developmental stage, rate, and quantity of protein synthesis, as well as the stability of the mRNA. (Theil et al.; BioFactors 4:87-93, (1993). Once identified and characterized, these regulatory regions may be utilized in gene therapylor protein purification schemes to obtain the desired amount and locations of protein synthesis or to inhibit, reduce/or prevent the synthesis of undesirable gene products.

In addition, ESTs containing the 5' ends of secretory protein genes or extended cDNAs which include 20 sequences adjacent to the sequences of the ESTs may include sequences useful as probes for chromosome mapping and the identification of individuals. Thus, there is a need to identify and characterize the sequences upstream of the 5' coding sequences of genes encoding secretory proteins.

Summary of the Invention

The present invention relates to purified, isolated, or recombinant extended cDNAs which encode secreted 25 proteins or fragments thereof. Preferably, the purified, isolated or recombinant cDNAs contain the entire open reading frame of their corresponding mRNAs, including a start codon and a stop codon. For example, the extended cDNAs may include nucleic acids encoding the signal peptide as well as the mature protein. Alternatively, the extended cDNAs may contain a fragment of the open reading frame. In some embodiments, the fragment may encode only the sequence of the mature protein. Alternatively, the fragment may encode only a portion of the mature protein. A further aspect of the 30 present invention is a nucleic acid which encodes the signal peptide of a secreted protein.

The present extended cDNAs were obtained using ESTs which include sequences derived from the authentic 5' ends of their corresponding mRNAs. As used herein the terms "EST" or "5' EST" refer to the short cDNAs which were used to obtain the extended cDNAs of the present invention. As used herein, the term "extended cDNA" refers to the cDNAs which include sequences adjacent to the 5' EST used to obtain them. The extended cDNAs may contain all or a

portion of the sequence of the EST which was used to obtain them. The term "corresponding mRNA" refers to the mRNA which was the template for the cDNA synthesis which produced the 5' EST. As used herein, the term "purified" does not require absolute purity: rather, it is intended as a relative definition. Individual extended cDNA clones isolated from a cDNA library have been conventionally purified to electrophoretic homogeneity. The sequences obtained from these clones could not be obtained directly either from the library or from total human DNA. The extended cDNA clones are not naturally occurring as such, but rather are obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The conversion of mRNA into a cDNA library involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection. Thus, creating a cDNA library from messenger RNA and subsequently isolating individual clones from that library results in an approximately 10⁴-10⁶ fold purification of the native message. Purification of starting material or natural material to at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

As used herein, the term "isolated" requires that the material be removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide present in a living animal is not isolated, but the same polynucleotide, separated from some or all of the coexisting materials in the natural system, is isolated.

As used herein, the term "recombinant" means that the extended cDNA is adjacent to "backbone" nucleic acid to which it is not adjacent in its natural environment. Additionally, to be "enriched" the extended cDNAs will represent 5% or more of the number of nucleic acid inserts in a population of nucleic acid backbone molecules. Backbone molecules according to the present invention include nucleic acids such as expression vectors, self-replicating nucleic acids, viruses, integrating nucleic acids, and other vectors or nucleic acids used to maintain or manipulate a nucleic acid insert of interest. Preferably, the enriched extended cDNAs represent 15% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. More preferably, the enriched extended cDNAs represent 50% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. In a highly preferred embodiment, the enriched extended cDNAs represent 90% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. "Stringent", "moderate," and "low" hybridization conditions are as defined in Example 29.

Unless otherwise indicated, a "complementary" sequence is fully complementary. Thus, extended cDNAs encoding secreted polypeptides or fragments thereof which are present in cDNA libraries in which one or more extended cDNAs encoding secreted polypeptides or fragments thereof make up 5% or more of the number of nucleic acid inserts in the backbone molecules are "enriched recombinant extended cDNAs" as defined herein. Likewise, extended cDNAs encoding secreted polypeptides or fragments thereof which are in a population of plasmids in which one or more extended cDNAs of the present invention have been inserted such that they represent 5% or more of the number of inserts in the plasmid backbone are "enriched recombinant extended cDNAs" as defined herein. However, extended

PCT/IB98/02122 WO 99/31236

cONAs encoding secreted polypeptides or fragments thereof which are in cDNA libraries in which the extended cONAs encoding secreted polypeptides or fragments thereof constitute less than 5% of the number of nucleic acid inserts in the population of backbone molecules, such as libraries in which backbone molecules having a cDNA insert encoding a secreted polypeptide are extremely rare, are not "enriched recombinant extended cDNAs."

.5.

In particular, the present invention relates to extended cDNAs which were derived from genes encoding secreted proteins. As used herein, a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal peptides in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g. soluble proteins), or partially (e.g. receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins which are 10 transported across the membrane of the endoplasmic reticulum.

5

Extended cDNAs encoding secreted proteins may include nucleic acid sequences, called signal sequences, which encode signal puptides which direct the extracellular secretion of the proteins encoded by the extended cDNAs. Generally, the signal peptides are located at the amino termini of secreted proteins.

Secreted proteins are translated by ribosomes associated with the "rough" endoplasmic reticulum. Generally, 15 secreted proteins are co-translationally transferred to the membrane of the endoplasmic reticulum. Association of the ribosome with the endoplasmic reticulum during translation of secreted proteins is mediated by the signal peptide. The signal peptide is typically cleaved following its co-translational entry into the endoplasmic reticulum. After delivery to the endoplasmic reticulum, secreted proteins may proceed through the Golgi apparatus. In the Golgi apparatus, the proteins may undergo post-translational modification before entering secretory vesicles which transport them across the 20 cell membrane.

The extended cDNAs of the present invention have several important applications. For example, they may be used to express the entire secreted protein which they encode. Alternatively, they may be used to express portions of the secreted protein. The portions may comprise the signal peptides encoded by the extended cDNAs or the mature proteins encoded by the extended cDNAs (i.e. the proteins generated when the signal peptide is cleaved off). The 25 portions may also comprise polypeptides having at least 10 consecutive amino acids encoded by the extended cDNAs. Alternatively, the portions may comprise at least 15 consecutive amino acids encoded by the extended cDNAs. In some embodiments, the portions may comprise at least 25 consecutive amino acids encoded by the extended cDNAs. In other embodiments, the portions may comprise at least 40 amino acids encoded by the extended cDNAs.

Antibodies which specifically recognize the entire secreted proteins encoded by the extended cDNAs or 30 fragments thereof having at least 10 consecutive amino acids, at least 15 consecutive amino acids, at least 25 consecutive amino acids, or at least 40 consecutive amino acids may also be obtained as described below. Antibodies which specifically recognize the mature protein generated when the signal peptide is cleaved may also be obtained as described below. Similarly, antibodies which specifically recognize the signal peptides encoded by the extended cDNAs may also be obtained.

In some embodiments, the extended cDNAs include the signal sequence. In other embodiments, the extended cDNAs may include the full coding sequence for the mature protein (i.e. the protein generated when the signal polypeptide is cleaved off). In addition, the extended cDNAs may include regulatory regions upstream of the translation start site or downstream of the stop codon which control the amount, location, or developmental stage of gene expression. As discussed above, secreted proteins are therapeutically important. Thus, the proteins expressed from the cDNAs may be useful in treating or controlling a variety of human conditions. The extended cDNAs may also be used to obtain the corresponding genomic DNA. The term "corresponding genomic DNA" refers to the genomic DNA which encodes mRNA which includes the sequence of one of the strands of the extended cDNA in which thymidine residues in the sequence of the extended cDNA are replaced by uracil residues in the mRNA.

The extended cDNAs or genomic DNAs obtained therefrom may be used in forensic procedures to identify individuals or in diagnostic procedures to identify individuals having genetic diseases resulting from abnormal expression of the genes corresponding to the extended cDNAs. In addition, the present invention is useful for constructing a high resolution map of the human chromosomes.

The present invention also relates to secretion vectors capable of directing the secretion of a protein of
interest. Such vectors may be used in gene therapy strategies in which it is desired to produce a gene product in one cell
which is to be delivered to another location in the body. Secretion vectors may also facilitate the purification of desired
proteins.

The present invention also relates to expression vectors capable of directing the expression of an inserted gene in a desired spatial or temporal manner or at a desired level. Such vectors may include sequences upstream of the extended cDNAs such as promoters or upstream regulatory sequences.

In addition, the present invention may also be used for gene therapy to control or treat genetic diseases. Signal peptides may also be fused to heterologous proteins to direct their extracellular secretion.

One embodiment of the present invention is a purified or isolated nucleic acid comprising the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary thereto. In one aspect of this embodiment, the nucleic acid is recombinant.

Another embodiment of the present invention is a purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 40-140 and 242-377 or one of the sequences complementary thereto. In one aspect of this embodiment, the nucleic acid comprises at least 15, 25, 30, 40, 50, 75, or 100 consecutive bases of one of the sequences of SEQ ID NOs: 40-140 and 242-377 or one of the sequences complementary thereto. The nucleic acid may be a recombinant nucleic acid.

Another embodiment of the present invention is a purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEO ID NOs: 40-140 and 242-377 or a sequence complementary to one of the sequences of SEO ID NOs: 40-140 and 242-377. In one aspect of this embodiment, the nucleic acid is recombinant.

25

Another embodiment of the present invention is a purified or isolated nucleic acid comprising the full coding sequences of one of SEO ID NOs: 40-140 and 242-377, wherein the full coding sequence optionally comprises the sequence encoding signal peptide as well as the sequence encoding mature protein. In a preferred embodiment, the isolated or purified nucleic acid comprises the full coding sequence of one of SEO ID Nos. 40, 42-44, 46, 48, 49, 51, 53, 60, 62-72, 76-78, 80-83, 85-88, 90, 93, 94, 97, 99-102, 104, 107-125, 127, 132, 135-138, 140 and 242-377 wherein the full coding sequence comprises the sequence encoding signal peptide and the sequence encoding mature protein. In one aspect of this embodiment, the nucleic acid is recombinant.

A further embodiment of the present invention is a purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40-140 and 242-377 which encode a mature protein. In a preferred embodiment, the purified or isolated nucleic acid comprises the nucleotides of one of SEQ ID NOs: 40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode a mature protein. In one aspect of this embodiment, the nucleic acid is recombinant.

Yet another embodiment of the present invention is a purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40-140 and 242-377 which encode the signal peptide. In a preferred embodiment, the purified or isolated nucleic acid comprises the nucleotides of SEQ ID NOs: 40, 42-46, 48, 49, 51, 53, 57, 60, 62-73, 76-78, 80-83, 85-88, 90, 93-95, 97, 99-102, 104, 107-125, 127, 128, 130, 132, 134-140 and 242-377 which encode the signal peptide. In one aspect of this embodiment, the nucleic acid is recombinant.

Another embodiment of the present invention is a purified or isolated nucleic acid encoding a polypeptide having the sequence of one of the sequences of SEQ ID NOs: 141-241 and 378-513. $-a_{\rm crit}$

Another embodiment of the present invention is a purified or isolated nucleic acid encoding a polypeptide having the sequence of a mature protein included in one of the sequences of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the purified or isolated nucleic acid encodes a polypeptide having the sequence of a mature protein included in one of the sequences of SEQ ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.

Another embodiment of the present invention is a purified or isolated nucleic acid encoding a polypeptide having the sequence of a signal peptide included in one of the sequences of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the purified or isolated nucleic acid encodes a polypeptide having the sequence of a signal peptide included in one of the sequences of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.

Yet another embodiment of the present invention is a purified or isolated protein comprising the sequence of one of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is a purified or isolated polypeptide comprising at least 10 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In one aspect of this embodiment, the purified or isolated polypeptide comprises at least 15, 20, 25, 35, 50, 75, 100, 150 or 200 consecutive

amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In still another aspect, the purified or isolated polypeptide comprises at least 25 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is an isolated or purified polypeptide comprising a signal peptide of one of the polypeptides of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the isolated or purified polypeptide comprises a signal peptide of one of the polypeptides of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.

Yet another embodiment of the present invention is an isolated or purified polypeptide comprising a mature protein of one of the polypeptides of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the isolated or purified polypeptide comprises a mature protein of one of the polypeptides of SEQ ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.

A further embodiment of the present invention is a method of making a protein comprising one of the sequences of SEQ ID NO: 141-241 and 378-513, comprising the steps of obtaining a cDNA comprising one of the sequences of sequence of SEQ ID NO: 40-140 and 242-227, inserting the cDNA in an expression vector such that the cDNA is operably linked to a promoter, and introducing the expression vector into a host cell whereby the host cell produces the protein encoded by said cDNA. In one aspect of this embodiment, the method further comprises the step of isolating the protein.

Another embodiment of the present invention is a protein obtainable by the method described in the preceding paragraph.

Another embodiment of the present invention is a method of making a protein comprising the amino acid sequence of the mature protein contained in one of the sequences of SEQ ID NO: 141-241 and 378-513, comprising the steps of obtaining a cDNA comprising one of the nucleotides sequence of sequence of SEQ ID NO: 40-140 and 242-377 which encode for the mature protein, inserting the cDNA in an expression vector such that the cDNA is operably linked to a promoter, and introducing the expression vector into a host cell whereby the host cell produces the mature protein encoded by the cDNA. In one aspect of this embodiment, the method further comprises the step of isolating the protein.

Another embodiment of the present invention is a mature protein obtainable by the method described in the 30 preceding paragraph.

In a preferred embodiment, the above method comprises a method of making a protein comprising the amino acid sequence of the mature protein contained in one of the sequences of SEO ID NO: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513, comprising the steps of obtaining a cDNA comprising one of the nucleotides sequence of sequence of SEO ID NO:

40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode for the mature protein, inserting the cDNA in an expression vector such that the cDNA is operably linked to a promoter, and introducing the expression vector into a host cell whereby the host cell produces the mature protein encoded by the cDNA. In one aspect of this embodiment, the method further comprises the step of isolating the protein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary thereto described herein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the full coding sequences of one of SEQ ID NOs: 40-140 and 242-377, wherein the full coding sequence comprises the sequence encoding signal peptide and the sequence encoding mature protein described herein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID NOs: 40-140 and 242-377 which encode a mature protein which are described herein. Preferably, the host cell contains the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID NOs: 40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode a mature protein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID NOs: 40-140 and 242-377 which encode the signal peptide which are described herein. Preferably, the host cell contains the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID Nos.: 40, 42-46, 48, 49, 51, 53, 57, 60, 62-73, 76-78, 80-83, 85-88, 90, 93-95, 97, 99-102, 104, 107-125, 127, 128, 130, 132, 134-140 and 242-377 which encode the signal peptide.

Another embodiment of the present invention is a purified or isolated antibody capable of specifically binding to a protein having the sequence of one of SEQ ID NOs: 141-241 and 378-513. In one aspect of this embodiment, the antibody is capable of binding to a polypeptide comprising at least 10 consecutive amino acids of the sequence of one of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is an array of cDNAs or fragments thereof of at least 15 nucleotides in length which includes at least one of the sequences of SEQ ID NOs: 40-140 and 242-377, or one of the sequences complementary to the sequences of SEQ ID NOs: 40-140 and 242-377, or a fragment thereof of at least 15 consecutive nucleotides. In one aspect of this embodiment, the array includes at least two of the sequences of SEQ ID NOs: 40-140 and 242-377, the sequences complementary to the sequences of SEQ ID NOs: 40-140 and 242-377, or fragments thereof of at least 15 consecutive nucleotides. In another aspect of this embodiment, the array includes at least five of the sequences of SEQ ID NOs: 40-140 and 242-377, the sequences complementary to the sequences of SEQ ID NOs: 40-140 and 242-377, or fragments thereof of at least 15 consecutive nucleotides.

A further embodiment of the invention encompasses purified polynucleotides comprising an insert from a clone deposited in a deposit having an accession number selected from the group consisting of the accession numbers listed in Table VI or a fragment thereof comprising a contiguous span of at least 8, 10, 12, 15, 20, 25, 40, 60, 100, or 200 nucleotides of said insert. An additional embodiment of the invention encompasses purified polypeptides which comprise, consist of, or consist essentially of an amino acid sequence encoded by the insert from a clone deposited in a deposit having an accession number selected from the group consisting of the accession numbers listed in Table VI, as well as polypeptides which comprise a fragment of said amino acid sequence consisting of a signal peptide, a mature protein, or a contiguous span of at least 5, 8, 10, 12, 15, 20, 25, 40, 60, 100, or 200 amino acids encoded by said insert.

An additional embodiment of the invention encompasses purified polypeptides which comprise a contiguous span of at least 5, 8, 10, 12, 15, 20, 25, 40, 60, 100, or 200 amino acids of SEQ ID NOs: 158, 174, 175, 196, 226, 231, 232, wherein said contiguous span comprises at least one of the amino acid positions which was not shown to be identical to a public sequence in any of Figures 11 to 15. Also encompassed by the invention are purified polynuculeotides encoding said polypeptides.

15

10

Brief Description of the Drawings

the mRNAs from which they are derived.

Figure 2 is an analysis of the 43 amino terminal amino acids of all human SwissProt proteins to determine the 20 frequency of false positives and false negatives using the techniques for signal peptide identification described herein.

Figure 3 shows the distribution of von Heijne scores for 5' ESTs in each of the categories described herein and the probability that these 5' ESTs encode a signal peotide.

Figure 4 shows the distribution of 5' ESTs in each category and the number of 5' ESTs in each category having a given minimum von Heijne's score.

Figure 5 shows the tissues from which the mRNAs corresponding to the 5' ESTs in each of the categories described herein were obtained.

Figure 6 illustrates a method for obtaining extended cDNAs.

Figure 7 is a map of pED6dpc2. pED6dpc2 is derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning. SSt cDNAs are cloned between EcoRt and Not1. PED vectors are described in Kaufman et al. 30 (1991), NAR 19: 4485-4490.

Figure 8 provides a schematic description of the promoters solated and the way they are assembled with the corresponding 5' tags.

Figure 9 describes the transcription factor binding sites present in each of these promoters.

Figure 10 is an alignment of the protein of SEQ ID NO: 217 with the human protein TFAR19 that may play a role in apoptosis (Genbank accession number AF014955, SEQ ID NO: 516).

Figure 11 is an alignment of the proteins of SEQ ID NOs: 174, 175 and 232 with a human secreted protein (Genseq accession number W36955, SEQ ID NO: 517).

Figure 12 is an alignment of the protein of SEQ ID NO: 231 with the human E25 protein (Genbank accession number AF038953, SEQ ID NO: 515).

Figure 13 is an alignment of the protein of SEQ ID NO: 196 with the human seventransmembrane protein (Genbank accession number Y11395, SEQ ID NO: 518).

Figure 14 is an alignment of the protein of SEQ ID NOs: 158 with the murine subunit 7a of the COP9 complex 10 (Genbank accession number AF071316, SEQ ID NO: 519).

Figure 15 is an alignment of the protein of SEQ ID NO: 226 with the bovine subunit B14.5B of the NADHubiquinone oxidureductase complex (Arizmendi *et al, FEBS Lett.*, 313 : 80-84 (1992) and Swissprot accession -number Q02827, SEQ ID NO: 514).

Detailed Description of the Preferred Embodiment

15 I. Obtaining 5' ESTs

The present extended cDNAs were obtained using 5' ESTs which were isolated as described below.

A. Chemical Methods for Obtaining mRNAs having Intact 5' Ends

In order to obtain the 5' ESTs used to obtain the extended cDNAs of the present invention, mRNAs having intact 5' ends must be obtained. Currently, there are two approaches for obtaining such mRNAs. One of these 20 approaches is a chemical modification method involving derivatization of the 5' ends of the mRNAs and selection of the derivatized mRNAs. The 5' ends of eucaryotic mRNAs possess a structure referred to as a "cap" which comprises a guanosine methylated at the 7 position. The cap is joined to the first transcribed base of the mRNA by a 5', 5'. triphosphate bond. In some instances, the 5' guanosine is methylated in both the 2 and 7 positions. Rarely, the 5' quanosine is trimethylated at the 2, 7 and 7 positions. In the chemical method for obtaining mRNAs having intact 5' 25 ends, the 5' cap is specifically derivatized and coupled to a reactive group on an immobilizing substrate. This specific derivatization is based on the fact that only the ribose linked to the methylated guanosine at the 5' end of the mRNA and the ribose linked to the base at the 3' terminus of the mRNA, possess 2', 3' cis diols. Optionally, where the 3' terminal ribose has a 2', 3'-cis diol, the 2', 3'-cis diol at the 3' end may be chemically modified, substituted, converted, or eliminated, leaving only the ribose linked to the methylated guanosine at the 5' end of the mRNA with a 2', 3'-cis diol. A 30 variety of techniques are available for eliminating the 2', 3'-cis diol on the 3' terminal ribose. For example, controlled alkaline hydrolysis may be used to generate mRNA fragments in which the 3' terminal ribose is a 3'-phosphate, 2'phosphate or (2', 3') cyclophosphate. Thereafter, the fragment which includes the original 3' ribose may be eliminated from the mixture through chromatography on an oligo-dT column. Alternatively, a base which lacks the 2', 3'-cis diol

may be added to the 3' end of the mRNA using an RNA ligase such as T4 RNA ligase. Example 1 below describes a method for ligation of pCp to the 3' end of messenger RNA.

EXAMPLE 1

Ligation of the Nucleoside Diphosphate pCp to the 3' End of Messenger RNA

5 1 μg of RNA was incubated in a final reaction medium of 10 μl in the presence of 5 U of T₄ phage RNA ligase in the buffer provided by the manufacturer (Gibco · BRL), 40 U of the RNase inhibitor RNasin (Promega) and, 2 μl of ³²pCp (Amersham #PB 10208).

The incubation was performed at 37°C for 2 hours or overnight at 7-8°C.

Following modification or elimination of the 2', 3'-cis diol at the 3' ribose, the 2', 3'-cis diol present at the 5' end of the mRNA may be oxidized using reagents such as NaBH, NaBH₃CN, or sodium periodate, thereby converting the 2', 3'-cis diol to a dialdehyde. Example 2 describes the oxidation of the 2', 3'-cis diol at the 5' end of the mRNA with sodium periodate.

EXAMPLE 2

Oxidation of 2', 3'-cis diol at the 5' End of the mRNA

- oligoribonucleotide of 46 nucleotides were treated as follows. The oligoribonucleotides were produced by in vitro transcription using the transcription kit "AmpliScribe T7" (Epicentre Technologies). As indicated below, the DNA template for the RNA transcript contained a single cytosine. To synthesize the uncapped RNA, all four NTPs were included in the in vitro transcription reaction. To obtain the capped RNA, GTP was replaced by an analogue of the cap, m7G(5')ppp(5')G. This compound, recognized by polymerase, was incorporated into the 5' end of the nascent transcript during the step of initiation of transcription but was not capable of incorporation during the extension step.

 Consequently, the resulting RNA contained a cap at its 5' end. The sequences of the oligoribonucleotides produced by the in vitro transcription reaction were:
 - +Cap:
- 25 5'm7GpppGCAUCCUACUCCCAUCCAAUUCCACCCUAACUCCUCCCAUCUCCAC-3' (SEQ ID NO:1)
 - ·Cap:
 - 5'-pppGCAUCCUACUCCCAUCCAAUUCCACCCUAACUCCUCCCAUCUCCAC-3' (SEQ ID NO:2)

The oligoribonucleotides were dissolved in 9 μ l of acetate buffer (0.1 M sodium acetate, pH 5.2) and 3 μ l of freshly prepared 0.1 M sodium periodate solution. The mixture was incubated for 1 hour in the dark at 4°C or room temperature. Thereafter, the reaction was stopped by adding 4 μ l of 10% ethylene glycol. The product was ethanol precipitated, resuspended in 10 μ l or more of water or appropriate buffer and dialyzed against water.

The resulting aldehyde groups may then be coupled to molecules having a reactive amine group, such as hydrazine, carbazide, thiocarbazide or semicarbazide groups, in order to facilitate enrichment of the 5' ends of the mRNAs. Molecules having reactive amine groups which are suitable for use in selecting mRNAs having intact 5' ends

include avidin, proteins, antibodies, vitamins, ligands capable of specifically binding to receptor molecules, or oligonucleotides. Example 3 below describes the coupling of the resulting dialdehyde to biotin.

EXAMPLE 3

Coupling of the Dialdehyde with Biotin

5 The oxidation product obtained in Example 2 was dissolved in 50 μl of sodium acetate at a pH of between 5 and 5.2 and 50 μl of freshly prepared 0.02 M solution of biotin hydrazide in a methoxyethanol/water mixture (1:1) of formula:

In the compound used in these experiments, n = 5. However, it will be appreciated that other commercially available hydrazides may also be used, such as molecules of the formula above in which n varies from 0 to 5.

The mixture was then incubated for 2 hours at 37°C. Following the incubation, the mixture was precipitated with ethanol and dialyzed against distilled water.

Example 4 demonstrates the specificity of the biotinylation reaction.

15

EXAMPLE 4

Specificity of Biotinylation

The specificity of the biotinylation for capped mRNAs was evaluated by gel electrophoresis of the following samples:

Sample 1. The 46 nucleotide uncapped in vitro transcript prepared as in Example 2 and labeled with ²²pCp as 20 described in Example 1.

Sample 2. The 46 nucleotide uncapped in vitro transcript prepared as in Example 2, labeled with ¹²pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.

Sample 3. The 47 nucleotide capped in vitro transcript prepared as in Example 2 and labeled with ³²pCp as described in Example 1.

Sample 4. The 47 nucleotide capped in vitro transcript prepared as in Example 2, labeled with ³²pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.

Samples 1 and 2 had indentical migration rates, demonstrating that the uncapped RNAs were not oxidized and 30 biotinylated. Sample 3 migrated more slowly than Samples 1 and 2, while Sample 4 exhibited the slowest migration.

The difference in migration of the RNAs in Samples 3 and 4 demonstrates that the capped RNAs were specifically biotinylated.

In some cases, mRNAs having intact 5' ends may be enriched by binding the molecule containing a reactive amine group to a suitable solid phase substrate such as the inside of the vessel containing the mRNAs, magnetic beads, 5 chromatography matrices, or nylon or nitrocellulose membranes. For example, where the molecule having a reactive amine group is biotin, the solid phase substrate may be coupled to avidin or streptavidin. Alternatively, where the molecule having the reactive amine group is an antibody or receptor ligand, the solid phase substrate may be coupled to the cognate antigen or receptor. Finally, where the molecule having a reactive amine group comprises an oligonucleotide, the solid phase substrate may comprise a complementary oligonucleotide.

The mRNAs having intact 5' ends may be released from the solid phase following the enrichment procedure. For example, where the dialdehyde is coupled to biotin hydrazide and the solid phase comprises streptavidin, the mRNAs may be released from the solid phase by simply heating to 95 degrees Celsius in 2% SDS. In some methods, the molecule having a reactive amine group may also be cleaved from the mRNAs having intact 5' ends following enrichment. Example 5 describes the capture of biotinylated mRNAs with streptavidin coated beads and the release of the 15 biotinylated mRNAs from the beads following enrichment.

EXAMPLE 5 - ខ្មែរប្រទេស

Capture and Release of Biotinylated mRNAs Using Strepatividin Coated Beads

The streptavidin-coated magnetic beads were prepared according to the manufacturer's instructions (CPG Inc., USA). The biotinylated mRNAs were added to a hybridization buffer (1.5 M NaCl, pH 5 - 6). After incubating for 30 20 minutes, the unbound and nonbiotinylated material was removed. The beads were washed several times in water with 1% SDS. The beads obtained were incubated for 15 minutes at 95°C in water containing 2% SDS.

Example 6 demonstrates the efficiency with which biotinylated mRNAs were recovered from the streptavidin coated beads.

EXAMPLE 6

25 Efficiency of Recovery of Biotinylated mRNAs

The efficiency of the recovery procedure was evaluated as follows. RNAs were labeled with ¹²pCp, oxidized, biotinylated and bound to streptavidin coated beads as described above. Subsequently, the bound RNAs were incubated for 5, 15 or 30 minutes at 95°C in the presence of 2% SDS.

The products of the reaction were analyzed by electrophoresis on 12% polyacrylamide gels under denaturing 30 conditions (7 M urea). The gels were subjected to autoradiography. During this manipulation, the hydrazone bonds were not reduced.

Increasing amounts of nucleic acids were recovered as incubation times in 2% SDS increased, demonstrating that biotinylated mRNAs were efficiently recovered.

In an alternative method for obtaining mRNAs having intact 5' ends, an oligonucleotide which has been derivatized to contain a reactive amine group is specifically coupled to mRNAs having an intact cap. Preferably, the 3' end of the mRNA is blocked prior to the step in which the aldehyde groups are joined to the derivatized oligonucleotide, as described above, so as to prevent the derivatized oligonucleotide from being joined to the 3' end of the mRNA. For example, pCp may be attached to the 3' end of the mRNA using T4 RNA ligase. However, as discussed above, blocking the 3' end of the mRNA is an optional step. Derivatized oligonucleotides may be prepared as described below in Example 7.

EXAMPLE 7

Derivatization of the Oligonucleotide

An oligonucleotide phosphorylated at its 3' end was converted to a 3' hydrazide in 3' by treatment with an aqueous solution of hydrazine or of dihydrazide of the formula H₂N(R1)NH₂ at about 1 to 3 M, and at pH 4.5, in the presence of a carbodiimide type agent soluble in water such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide at a final concentration of 0.3 M at a temperature of 8°C overnight.

The derivatized oligonucleotide was then separated from the other agents and products using a standard technique for isolating oligonucleotides.

As discussed above, the mRNAs to be enriched may be treated to eliminate the 3' OH groups which may be present thereon. This may be accomplished by enzymatic ligation of sequences lacking a 3' OH, such as pCp, as described above in Example 1. Alternatively, the 3' OH groups may be eliminated by alkaline hydrolysis as described in Example 8 below.

20

EXAMPLE 8

Alkaline Hydrolysis of mRNA

The mRNAs may be treated with alkaline hydrolysis as follows. In a total volume of 100µJ of 0.1N sodium hydroxide, 1.5µg mRNA is incubated for 40 to 60 minutes at 4°C. The solution is neutralized with acetic acid and precipitated with ethanol.

Following the optional elimination of the 3' OH groups, the diol groups at the 5' ends of the mRNAs are oxidized as described below in Example 9.

EXAMPLE 9

Oxidation of Diols

Up to 1 OD unit of RNA was dissolved in 9 µl of buffer (0.1 M sodium acetate, pH 6-7 or water) and 3 µl of freshly prepared 0.1 M sodium periodate solution. The reaction was incubated for 1 h in the dark at 4°C or room temperature. Following the incubation, the reaction was stopped by adding 4 µl of 10% ethylene glycol. Thereafter the mixture was incubated at room temperature for 15 minutes. After ethanol precipitation, the product was resuspended in 10µl or more of water or appropriate buffer and dialyzed against water.

Following oxidation of the diol groups at the 5' ends of the mRNAs, the derivatized oligonucleotide was joined to the resulting aldehydes as described in Example 10.

EXAMPLE 10

Reaction of Aldehydes with Derivatized Oligonucleotides

The oxidized mRNA was dissolved in an acidic medium such as 50 µl of sodium acetate pH 4-6. 50 µl of a solution of the derivatized oligonucleotide was added such that an mRNA:derivatized oligonucleotide ratio of 1:20 was obtained and mixture was reduced with a borohydride. The mixture was allowed to incubate for 2 h at 37°C or overnight (14 h) at 10°C. The mixture was ethanol precipitated, resuspended in 10µl or more of water or appropriate buffer and dialyzed against distilled water. If desired, the resulting product may be analyzed using acrylamide gel electrophoresis, HPLC analysis, or other conventional techniques.

Following the attachment of the derivatized oligonucleotide to the mRNAs, a reverse transcription reaction may be performed as described in Example 11 below.

EXAMPLE 11

Reverse Transcription of mRNAs

An oligodeoxyribonucleotide was derivatized as follows. 3 OD units of an oligodeoxyribonucleotide of sequence ATCAAGAATTCGCACGAGACCATTA (SEQ ID NO:3) having 5' OH and 3' P ends were dissolved in 70 µl of a 1.5 M hydroxybenzotriazole solution, pH 5.3, prepared in dimethylformamide/water (75:25) containing 2 µg of 1 ethyl-3-(3-dimethylaminopropyl)carbodiimide. The mixture was incubated for 2 h 30 min at 22°C. The mixture was then precipitated twice in LiClO₄/acetone. The pellet was resuspended in 200 µl of 0.25 M hydrazine and incubated at 8°C from 3 to 14 h. Following the hydrazine reaction, the mixture was precipitated twice in LiClO₄/acetone.

The messenger RNAs to be reverse transcribed were extracted from blocks of placenta having sides of 2 cm which had been stored at -80°C. The mRNA was extracted using conventional acidic phenol techniques. Oligo-dT chromatography was used to purify the mRNAs. The integrity of the mRNAs was checked by Northern-blotting.

The dial groups on 7 µg of the placental mRNAs were oxidized as described above in Example 9. The

derivatized oligonucleotide was joined to the mRNAs as described in Example 10 above except that the precipitation step was replaced by an exclusion chromatography step to remove derivatized oligodeoxyribonucleotides which were not joined to mRNAs. Exclusion chromatography was performed as follows:

10 ml of AcA34 (BioSepra#230151) gel were equilibrated in 50 ml of a solution of 10 mM Tris pH 8.0, 300 mM NaCl, 1 mM EDTA, and 0.05% SDS. The mixture was allowed to sediment. The supernatant was eliminated and the gel was resuspended in 50 ml of buffer. This procedure was repeated 2 or 3 times.

A glass bead (diameter 3 mm) was introduced into a 2 ml disposable pipette (length 25 cm). The pipette was filled with the gel suspension until the height of the gel stabilized at 1 cm from the top of the pipette. The column was then equilibrated with 20 ml of equilibration buffer (10 mM Tris HCl pH 7.4, 20 mM NaCl).

10 μ l of the mRNA which had been reacted with the derivatized oligonucleotide were mixed in 39 μ l of 10 mM urea and 2 μ l of blue-glycerol buffer, which had been prepared by dissolving 5 mg of bromophenol blue in 60% glycerol (v/v), and passing the mixture through a filter with a filter of diameter 0.45 μ m.

The column was loaded. As soon as the sample had penetrated, equilibration buffer was added. 100 µl

fractions were collected. Derivatized oligonucleotide which had not been attached to mRNA appeared in fraction 16 and later fractions. Fractions 3 to 15 were combined and precipitated with ethanol.

The mRNAs which had been reacted with the derivatized oligonucleotide were spotted on a nylon membrane and hybridized to a radioactive probe using conventional techniques. The radioactive probe used in these hybridizations was an oligodeoxyribonucleotide of sequence TAATGGTCTCGTGCGAATTCTTGAT (SEQ ID NO:4) which was anticomplementary to the derivatized oligonucleotide and was labeled at its 5' end with ³²P. 1/10th of the mRNAs which had been reacted with the derivatized oligonucleotide was spotted in two spots on the membrane and the membrane was visualized by autoradiography after hybridization of the probe. A signal was observed, indicating that the derivatized oligonucleotide had been joined to the mRNA.

The remaining 9/10 of the mRNAs which had been reacted with the derivatized oligonucleotide was reverse transcribed as follows. A reverse transcription reaction was carried out with reverse transcriptase following the manufacturer's instructions. To prime the reaction, 50 pmol of nonamers with random sequence were used.

A portion of the resulting cDNA was spotted on a positively charged nylon membrane using conventional methods. The cDNAs were spotted on the membrane after the cDNA:RNA heteroduplexes had been subjected to an alkaline hydrolysis in order to eliminate the RNAs. An oligonucleotide having a sequence identical to that of the derivatized oligonucleotide was labeled at its 5' end with ³²P and hybridized to the cDNA blots using conventional techniques. Single-stranded cDNAs resulting from the reverse transcription reaction were spotted on the membrane. As controls, the blot contained 1 pmol, 100 fmol, 50 fmol, 10 fmol and 1 fmol respectively of a control oligodeoxyribonucleotide of sequence identical to that of the derivatized oligonucleotide. The signal observed in the spots containing the cDNA indicated that approximately 15 fmol of the derivatized oligonucleotide had been reverse transcribed.

These results demonstrate that the reverse transcription can be performed through the cap and, in particular, that reverse transcriptase crosses the 5'-P-P-5' bond of the cap of eukaryotic messenger RNAs.

The single stranded cDNAs obtained after the above first strand synthesis were used as template for PCR reactions. Two types of reactions were carried out. First, specific amplification of the mRNAs for the alpha globin, dehydrogenase, pp15 and elongation factor E4 were carried out using the following pairs of oligodeoxyribonucleotide primers.

alpha-globin

25

30

GLO-S: CCG ACA AGA CCA ACG TCA AGG CCG C (SEQ ID NO:5)

GLO-As: TCA CCA GCA GGC AGT GGC TTA GGA G 3' (SEQ ID NO:6)

dehydrogenase

3 DH-S: AGT GAT TCC TGC TAC TTT GGA TGG C (SEQ ID NO:7)

3 DH-As: GCT TGG TCT TGT TCT GGA GTT TAG A (SEQ ID NO:8)

pp15

PP15-S: TCC AGA ATG GGA GAC AAG CCA ATT T (SEQ ID NO:9)

5 PP15-As: AGG GAG GAG GAA ACA GCG TGA GTC C (SEQ ID NO:10)

Elongation factor E4

EFA1-S: ATG GGA AAG GAA AAG ACT CAT ATC A (SEQ ID NO:11)

EF1A-As: AGC AGC AAC AAT CAG GAC AGC ACA G (SEQ ID NO:12)

Non specific amplifications were also carried out with the antisense (_As) oligodeoxyribonucleotides of the pairs described above and a primer chosen from the sequence of the derivatized oligodeoxyribonucleotide (ATCAAGAATTCGCACGAGACCATTA) (SEQ ID NO:13).

- A 1.5% agarose gel containing the following samples corresponding to the PCR products of reverse transcription was stained with ethidium bromide. (1/20th of the products of reverse transcription were used for each PCR reaction).
- Sample 1: The products of a PCR reaction using the globin primers of SEQ ID NOs 5 and 6 in the presence of cDNA.
 - Sample 2: The products of a PCR reaction using the globin primers of SEQ.(D.NOs 5 and 6 in the absence of added cDNA.
- Sample 3: The products of a PCR reaction using the dehydrogenase primers; of SEQ ID NOs 7 and 8 in the 20 presence of cDNA.
 - Sample 4: The products of a PCR reaction using the dehydrogenase primers of SEQ ID NOs 7 and 8 in the absence of added cDNA.
 - Sample 5: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the presence of cDNA.
- Sample 6: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the absence of added cDNA.
 - Sample 7: The products of a PCR reaction using the EIE4 primers of SEQ ID NOs 11 and 12 in the presence of added cDNA.
- Sample 8: The products of a PCR reaction using the EIE4 primers of SEQ ID NOs 11 and 12 in the absence of 30 added cDNA.
 - In Samples 1, 3, 5 and 7, a band of the size expected for the PCR product was observed, indicating the presence of the corresponding sequence in the cDNA population.
 - PCR reactions were also carried out with the antisense oligonucleotides of the globin and dehydrogenase primers (SEO ID NOs 6 and 8) and an oligonucleotide whose sequence corresponds to that of the derivatized

oligonucleotide. The presence of PCR products of the expected size in the samples corresponding to samples 1 and 3 above indicated that the derivatized oligonucleotide had been incorporated.

The above examples summarize the chemical procedure for enriching mRNAs for those having intact 5' ends.

Further detail regarding the chemical approaches for obtaining mRNAs having intact 5' ends are disclosed in

International Application No. W096/34981, published November 7, 1996.

Strategies based on the above chemical modifications to the 5' cap structure may be utilized to generate cDNAs which have been selected to include the 5' ends of the mRNAs from which they are derived. In one version of such procedures, the 5' ends of the mRNAs are modified as described above. Thereafter, a reverse transcription reaction is conducted to extend a primer complementary to the mRNA to the 5' end of the mRNA. Single stranded RNAs are eliminated to obtain a population of cDNA/mRNA heteroduplexes in which the mRNA includes an intact 5' end. The resulting heteroduplexes may be captured on a solid phase coated with a molecule capable of interacting with the molecule used to derivatize the 5' end of the mRNA. Thereafter, the strands of the heteroduplexes are separated to recover single stranded first cDNA strands which include the 5' end of the mRNA. Second strand cDNA synthesis may then proceed using conventional techniques. For example, the procedures disclosed in WO 96/34981 or in Carninci, P. et al. High-Efficiency Full-Length cDNA Cloning by Biotinylated CAP Trapper. Genomics 37:327-336 (1996) may be employed to select cDNAs which include the sequence derived from the 5' end of the coding sequence of the mRNA.

Following ligation of the oligonucleotide tag to the 5' cap of the mRNA, a reverse transcription reaction is conducted to extend a primer complementary to the mRNA to the 5' end of the mRNA. Following elimination of the RNA component of the resulting heteroduplex using standard techniques, second strand cDNA synthesis is conducted with a primer complementary to the oligonucleotide tag.

Figure 1 summarizes the above procedures for obtaining cDNAs which have been selected to include the 5' ends of the mRNAs from which they are derived.

B. Enzymatic Methods for Obtaining mRNAs having Intact 5' Ends

Other techniques for selecting cDNAs extending to the 5' end of the mRNA from which they are derived are fully enzymatic. Some versions of these techniques are disclosed in Dumas Milne Edwards J.B. (Doctoral Thesis of Paris VI University, Le clonage des ADNc complets: difficultes et perspectives nouvelles. Apports pour l'étude de la regulation de l'expression de la tryptophane hydroxylase de rat, 20 Dec. 1993), EPO 625572 and Kato et al. Construction of a Human Full-Length cDNA Bank. Gene 150:243-250 (1994).

Briefly, in such approaches, isolated mRNA is treated with alkaline phosphatase to remove the phosphate

30 groups present on the 5' ends of uncapped incomplete mRNAs. Following this procedure, the cap present on full length mRNAs is enzymatically removed with a decapping enzyme such as T4 polynucleotide kinase or tobacco acid pyrophosphatase. An oligonucleotide, which may be either a DNA oligonucleotide or a DNA-RNA hybrid oligonucleotide having RNA at its 3' end, is then ligated to the phosphate present at the 5' end of the decapped mRNA using T4 RNA

ligase. The oligonucleotide may include a restriction site to facilitate cloning of the cDNAs following their synthesis. Example 12 below describes one enzymatic method based on the doctoral thesis of Dumas.

EXAMPLE 12

Enzymatic Approach for Obtaining 5' ESTs

Twenty micrograms of PolyA + RNA were dephosphorylated using Calf Intestinal Phosphatase (Biolabs). After a phenol chloroform extraction, the cap structure of mRNA was hydrolysed using the Tobacco Acid Pyrophosphatase (purified as described by Shinshi et al., Biochemistry 15: 2185-2190, 1976) and a hemi 5'DNA/RNA-3' oligonucleotide having an unphosphorylated 5' end, a stretch of adenosine ribophosphate at the 3' end, and an EcoRI site near the 5' end was ligated to the 5'P ends of mRNA using the T4 RNA ligase (Biolabs). Oligonucleotides suitable for use in this 10 procedure are preferably 30-50 bases in length. Oligonucleotides having an unphosphorylated 5' end may be synthesized by adding a fluorochrome at the 5' end. The inclusion of a stretch of adenosine ribophosphates at the 3' end of the oligonucleotide increases ligation afficiency. It will be appreciated that the oligonucleotide may contain cloning sites other than EcoRI.

Following ligation of the oligonucleotide to the phosphate present at the 5' end of the decapped mRNA, first 15 and second strand cDNA synthesis may be carried out using conventional methods or those specified in EPO 625,572 and Kato et al. Construction of a Human Full-Length cDNA Bank. Gene 150:243-250 (1994), and Dumas Milne Edwards. supra. The resulting cDNA may then be ligated into vectors such as those disclosed in Kato et al. Construction of a Human Full-Length cDNA Bank. Gene 150:243-250 (1994) or other nucleic acid vectors known to those skilled in the art using techniques such as those described in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold 20 Spring Harbor Laboratory Press, 1989.

II. Characterization of 5' ESTs

The above chemical and enzymatic approaches for enriching mRNAs having intact 5' ends were employed to obtain 5' ESTs. First, mRNAs were prepared as described in Example 13 below.

EXAMPLE 13

25

Preparation of mRNA

Total human RNAs or PolyA + RNAs derived from 29 different tissues were respectively purchased from LABIMO and CLONTECH and used to generate 44 cDNA libraries as described below. The purchased RNA had been isolated from cells or tissues using acid guanidium thiocyanate-phenol-chloroform extraction (Chomczyniski, P and Sacchi, N., Analytical Biochemistry 162:156-159, 1987). PolyA - RNA was isolated from total RNA (LABIMO) by 30 two passes of oligodT chromatography, as described by Aviv and Leder (Aviv. H. and Leder, P., Proc. Natl. Acad. Sci. USA 69:1408-1412, 1972) in order to eliminate ribosomal RNA.

The quality and the integrity of the poly A+ were checked. Northern blots hybridized with a globin probe were used to confirm that the mRNAs were not degraded. Contamination of the PolyA + mRNAs by ribosomal sequences was checked using RNAs blots and a probe derived from the sequence of the 28S RNA. Preparations of mRNAs with less

1 3 1 25 D

16.18 aso 1

than 5% of ribosomal RNAs were used in library construction. To avoid constructing libraries with RNAs contaminated by exogenous sequences (prokaryotic or fungal), the presence of bacterial 16S ribosomal sequences or of two highly expressed mRNAs was examined using PCR.

Following preparation of the mRNAs, the above described chemical and/or the enzymatic procedures for enriching mRNAs having intact 5' ends discussed above were employed to obtain 5' ESTs from various tissues. In both approaches an oligonucleotide tag was attached to the cap at the 5' ends of the mRNAs. The oligonucleotide tag had an EcoRI site therein to facilitate later cloning procedures.

Following attachment of the oligonucleotide tag to the mRNA by either the chemical or enzymatic methods, the integrity of the mRNA was examined by performing a Northern blot with 200-500ng of mRNA using a probe complementary to the oligonucleotide tag.

EXAMPLE 14

cDNA Synthesis Using mRNA Templates Having Intact 5' Ends

For the mRNAs joined to oligonucleotide tags using both the chemical and enzymatic methods, first strand cDNA synthesis was performed using reverse transcriptase with random nonamers as primers. In order to protect internal EcoRI sites in the cDNA from digestion at later steps in the procedure, methylated dCTP was used for first strand synthesis. After removal of RNA by an alkaline hydrolysis, the first strand of cDNA was precipitated using isopropanol in order to eliminate residual primers.

For both the chemical and the enzymatic methods, the second strand of the cDNA was synthesized with a Klenow fragment using a primer corresponding to the 5'end of the ligated oligonucleotide described in Example 12.

20 Preferably, the primer is 20-25 bases in length. Methylated dCTP was also used for second strand synthesis in order to protect internal EcoRI sites in the cDNA from digestion during the cloning process.

Following cDNA synthesis, the cDNAs were cloned into pBlueScript as described in Example 15 below.

EXAMPLE 15

Insertion of cDNAs into BlueScript

Following second strand synthesis, the ends of the cDNA were blunted with T4 DNA polymerase (Biolabs) and the cDNA was digested with EcoRI. Since methylated dCTP was used during cDNA synthesis, the EcoRI site present in the tag was the only site which was hemi-methylated. Consequently, only the EcoRI site in the oligonucleotide tag was susceptible to EcoRI digestion. The cDNA was then size fractionated using exclusion chromatography (AcA, Biosepra). Fractions corresponding to cDNAs of more than 150 bp were pooled and ethanol precipitated. The cDNA was directionally cloned into the Smal and EcoRI ends of the phagemid pBlueScript vector (Stratagene). The ligation mixture was electroporated into bacteria and propagated under appropriate antibiotic selection.

Clones containing the oligonucleotide tag attached were selected as described in Example 16 below.

EXAMPLE 16

Selection of Clones Having the Oligonucleotide Tag Attached Thereto

The plasmid DNAs containing 5' EST libraries made as described above were purified (Qiagen). A positive selection of the tagged clones was performed as follows. Briefly, in this selection procedure, the plasmid DNA was converted to single stranded DNA using gene II endonuclease of the phage F1 in combination with an exonuclease (Chang et al., Gene 127:95-8, 1993) such as exonuclease III or T7 gene 6 exonuclease. The resulting single stranded DNA was then purified using paramagnetic beads as described by Fry et al., Biotechniques, 13: 124-131, 1992. In this procedure, the single stranded DNA was hybridized with a biotinylated oligonucleotide having a sequence corresponding to the 3' end of the oligonucleotide described in Example 13. Preferably, the primer has a length of 20-25 bases. Clones including a sequence complementary to the biotinylated oligonucleotide were captured by incubation with streptavidin coated magnetic beads followed by magnetic selection. After capture of the positive clones, the plasmid DNA was released from the magnetic beads and converted into double stranded DNA using a DNA polymerase such as the ThermoSequenase obtained from Amersham Pharmacia Biotech. Alternatively, protocols such as the Gene Trapper kit (Gibco BRL) may be used. The double stranded DNA was then electroporated into bacteria. The percentage of positive clones having the 5' tag oligonucleotide was estimated to typically rank between 90 and 98% using dot blot analysis.

Following electroporation, the libraries were ordered in 384-microtiter plates (MTP). A copy of the MTP was stored for future needs. Then the libraries were transferred into 96 MTP and sequenced as described below.

EXAMPLE 17

Sequencing of Inserts in Selected Clones

Plasmid inserts were first amplified by PCR on PE 9600 thermocyclers (Perkin-Elmer), using standard SETA-A and SETA-B primers (Genset SA), AmpliTaqGold (Perkin-Elmer), dNTPs (Boehringer), buffer and cycling conditions as recommended by the Perkin-Elmer Corporation.

PCR products were then sequenced using automatic ABI Prism 377 sequencers (Perkin Elmer, Applied Biosystems Division, Foster City, CA). Sequencing reactions were performed using PE 9600 thermocyclers (Perkin Elmer) with standard dye-primer chemistry and ThermoSequenase (Amersham Life Science). The primers used were either T7 or 21M13 (available from Genset SA) as appropriate. The primers were labeled with the JOE, FAM, ROX and TAMRA dyes. The dNTPs and ddNTPs used in the sequencing reactions were purchased from Boehringer. Sequencing buffer, reagent concentrations and cycling conditions were as recommended by Amersham.

Following the sequencing reaction, the samples were precipitated with EtOH, resuspended in formamide loading buffer, and loaded on a standard 4% acrylamide gel. Electrophoresis was performed for 2.5 hours at 3000V on an ABI 377 sequencer, and the sequence data were collected and analyzed using the ABI Prism DNA Sequencing

30 Analysis Software, version 2.1.2.

The sequence data from the 44 cDNA libraries made as described above were transferred to a proprietary database, where quality control and validation steps were performed. A proprietary base-caller ("Trace"), working using a Unix system automatically flagged suspect peaks, taking into account the shape of the peaks, the inter-peak resolution, and the noise level. The proprietary base-caller also performed an automatic trimming. Any stretch of 25 or

∙23∙

fewer bases having more than 4 suspect peaks was considered unreliable and was discarded. Sequences corresponding to cloning vector or ligation oligonucleotides were automatically removed from the EST sequences. However, the resulting EST sequences may contain 1 to 5 bases belonging to the above mentioned sequences at their 5' end. If needed, these can easily be removed on a case by case basis.

Thereafter, the sequences were transferred to the proprietary NETGENE™ Database for further analysis as described below.

5

20

Following sequencing as described above, the sequences of the 5' ESTs were entered in a proprietary database called NETGENETM for storage and manipulation. It will be appreciated by those skilled in the art that the data could be stored and manipulated on any medium which can be read and accessed by a computer. Computer readable media include magnetically readable media, optically readable media, or electronically readable media. For example, the computer readable media may be a hard disc, a floppy disc, a magnetic tape, CD-ROM, RAM, or ROM as well as other types of other media known to those skilled in the art.

In addition, the sequence data may be stored and manipulated in a variety of data processor programs in a variety of formats. For example, the sequence data may be stored as text in a word processing file, such as

MicrosoftWORD or WORDPERFECT or as an ASCII file in a variety of database programs familiar to those of skill in the art. Such as DB2, SYBASE, or ORACLE.

network, a server or other computer systems known to those skilled in the art. The computer or other system preferably includes the storage media described above, and a processor for accessing and manipulating the sequence data.

Once the sequence data has been stored it may be manipulated and searched to locate those stored sequences which contain a desired nucleic acid sequence or which encode a protein having a particular functional domain. For example, the stored sequence information may be compared to other known sequences to identify homologies, motifs implicated in biological function, or structural motifs.

Programs which may be used to search or compare the stored sequences include the MacPattern (EMBL),

25 BLAST, and BLAST2 program series (NCBI), basic local alignment search tool programs for nucleotide (BLASTN) and

peptide (BLASTX) comparisons (Altschul et al, J. Mol. Biol. 215: 403 (1990)) and FASTA (Pearson and Lipman, Proc.

Natl. Acad. Sci. USA. 85: 2444 (1988)). The BLAST programs then extend the alignments on the basis of defined

match and mismatch criteria.

Motifs which may be detected using the above programs include sequences encoding leucine zippers, helix-turn30 helix motifs, glycosylation sites, ubiquitination sites, alpha helices, and beta sheets, signal sequences encoding signal peptides which direct the secretion of the encoded proteins, sequences implicated in transcription regulation such as homeoboxes, acidic stretches, enzymatic active sites, substrate binding sites, and enzymatic cleavage sites.

Before searching the cDNAs in the NETGENE™ database for sequence motifs of interest, cDNAs derived from mRNAs which were not of interest were identified and eliminated from further consideration as described in Example 18 below.

EXAMPLE 18

5

25

Elimination of Undesired Sequences from Further Consideration

5' ESTs in the NETGENE™ database which were derived from undesired sequences such as transfer RNAs, ribosomal RNAs, mitochondrial RNAs, procaryotic RNAs, fungal RNAs, Alu sequences, L1 sequences, or repeat sequences were identified using the FASTA and BLASIN programs with the parameters listed in Table II.

To eliminate 5' ESTs encoding tRNAs from further consideration, the 5' EST sequences were compared to the 10 sequences of 1190 known tRNAs obtained from EMBL release 38, of which 100 were human. The comparison was performed using FASTA on both strands of the 5' ESTs. Sequences having more than 80% homology over more than 60 nucleotides were identified as tRNA. Of the 144,341 sequences screened, 26 were identified as tRNAs and eliminated from further consideration.

To eliminate 5' ESTs encoding rRNAs from further consideration, the 5' EST sequences were compared to the 15 sequences of 2497 known rRNAs obtained from EMBL release 38, of which 73 were human. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S - 108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as rRNAs. Of the 144,341 sequences screened, 3,312 were identified as rRNAs and eliminated from further consideration.

To eliminate 5' ESTs encoding mtRNAs from further consideration, the 5' EST sequences were compared to 20 the sequences of the two known mitochondrial genomes for which the entire genomic sequences are available and all sequences transcribed from these mitochondrial genomes including tRNAs, rRNAs, and mRNAs for a total of 38 sequences. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S = 108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as mtRNAs. Of the 144,341 sequences screened, 6,110 were identified as mtRNAs and eliminated from further consideration.

Sequences which might have resulted from exogenous contaminants were eliminated from further consideration by comparing the 5' EST sequences to release 46 of the EMBL bacterial and fungal divisions using BLASTN with the parameter S=144. All sequences having more than 90% homology over at least 40 nucleotides were identified as exogenous contaminants. Of the 42 cDNA libraries examined, the average percentages of procaryotic and fungal sequences contained therein were 0.2% and 0.5% respectively. Among these sequences, only one could be 30 identified as a sequence specific to fungi. The others were either fungal or procaryotic sequences having homologies with vertebrate sequences or including repeat sequences which had not been masked during the electronic comparison.

In addition, the 5' ESTs were compared to 6093 Alu sequences and 1115 L1 sequences to mask 5' ESTs containing such repeat sequences from further consideration. 5' ESTs including THE and MER repeats, SSTR sequences or satellite, micro-satellite, or telomeric repeats were also eliminated from further consideration. On average, 11.5% of

the sequences in the libraries contained repeat sequences. Of this 11.5%, 7% contained Alu repeats, 3.3% contained L1 repeats and the remaining 1.2% were derived from the other types of repetitive sequences which were screened. These percentages are consistent with those found in cDNA libraries prepared by other groups. For example, the cDNA libraries of Adams et al. contained between 0% and 7.4% Alu repeats depending on the source of the RNA which was used to prepare the cDNA library (Adams et al., Nature 377:174, 1996).

- The sequences of those 5' ESTs remaining after the elimination of undesirable sequences were compared with the sequences of known human mRNAs to determine the accuracy of the sequencing procedures described above.

EXAMPLE 19

Measurement of Sequencing Accuracy by Comparison to Known Sequences

To further determine the accuracy of the sequencing procedure described above, the sequences of 5' ESTs derived from known sequences were identified and compared to the known sequences. First, a FASTA analysis with overhangs shorter than 5 bp on both ends was conducted on the 5' ESTs to identify those matching an entry in the public human mRNA database. The 6655 5' ESTs which matched a known human mRNA were then realigned with their cognate mRNA and dynamic programming was used to include substitutions, insertions, and deletions in the list of "errors" which would be recognized. Errors occurring in the last 10 bases of the 5' EST sequences were ignored to avoid the inclusion of spurious cloning sites in the analysis of sequencing accuracy.

To determine the efficiency with which the above selection procedures select cDNAs which include the 5' ends of their corresponding mRNAs, the following analysis was performed.

EXAMPLE 20

Determination of Efficiency of 5' EST Selection

To determine the efficiency at which the above selection procedures isolated 5' ESTs which included sequences close to the 5' end of the mRNAs from which they were derived, the sequences of the ends of the 5' ESTs which were derived from the elongation factor 1 subunit α and ferritin heavy chain genes were compared to the known cDNA sequences for these genes. Since the transcription start sites for the elongation factor 1 subunit α and ferritin heavy chain are well characterized, they may be used to determine the percentage of 5' ESTs derived from these genes which included the authentic transcription start sites.

For both genes, more than 95% of the cDNAs included sequences close to or upstream of the 5' end of the 30 corresponding mRNAs.

To extend the analysis of the reliability of the procedures for isolating 5' ESTs from ESTs in the NETGENETM database, a similar analysis was conducted using a database composed of human mRNA sequences extracted from GenBank database release 97 for comparison. For those 5' ESTs derived from mRNAs included in the GeneBank database, more than 85% had their 5' ends close to the 5' ends of the known sequence. As some of the mRNA

sequences available in the GenBank database are deduced from genomic sequences, a 5' end matching with these sequences will be counted as an internal match. Thus, the method used here underestimates the yield of ESTs including the authentic 5' ends of their corresponding mRNAs.

The EST libraries made above included multiple 5' ESTs derived from the same mRNA. The sequences of such 5' ESTs were compared to one another and the longest 5' ESTs for each mRNA were identified. Overlapping cDNAs were assembled into continuous sequences (contigs). The resulting continuous sequences were then compared to public databases to gauge their similarity to known sequences, as described in Example 21 below.

EXAMPLE 21

Clustering of the 5' ESTs and Calculation of Novelty Indices for cDNA Libraries

For each sequenced EST library, the sequences were clustered by the 5' end. Each sequence in the library was compared to the others with BLASTN2 (direct strand, parameters S = 107). ESTs with High Scoring Segment Pairs (HSPs) at least 25 bp long, having 95% identical bases and beginning closer than 10 bp from each EST 5' end were grouped. The longest sequence found in the cluster was used as representative of the cluster. A global clustering between libraries was then performed leading to the definition of super-contios.

To assess the yield of new sequences within the EST libraries, a novelty rate (NR) was defined as: NR = 100 X (Number of new unique sequences found in the library/Total number of sequences from the library). Typically, novelty rating range between 10% and 41% depending on the tissue from which the EST library was obtained. For most of the libraries, the random sequencing of 5' EST libraries was pursued until the novelty rate reached 20%.

Following characterization as described above, the collection of 5' ESTs in NETGENETM was screened to 20 identify those 5' ESTs bearing potential signal sequences as described in Example 22 below.

EXAMPLE 22

Identification of Potential Signal Sequences in 5' ESTs

The 5' ESTs in the NETGENETM database were screened to identify those having an uninterrupted open reading frame (ORF) longer than 45 nucleotides beginning with an ATG codon and extending to the end of the EST.

25 Approximately half of the cDNA sequences in NETGENETM contained such an ORF. The ORFs of these 5' ESTs were searched to identify potential signal motifs using slight modifications of the procedures disclosed in Von Heijne, G. A New Method for Predicting Signal Sequence Cleavage Sites. Nucleic Acids Res. 14:4683-4690 (1986). Those 5' EST sequences encoding a 15 amino acid long stretch with a score of at least 3.5 in the Von Heijne signal peptide identification matrix were considered to possess a signal sequence. Those 5' ESTs which matched a known human mRNA or EST sequence and had a 5' end more than 20 nucleotides downstream of the known 5' end were excluded from further analysis. The remaining cDNAs having signal sequences therein were included in a database called SIGNALTAGTM.

To confirm the accuracy of the above method for identifying signal sequences, the analysis of Example 23 was performed.

EXAMPLE 23

Confirmation of Accuracy of Identification of Potential Signal Sequences in 5' ESTs

The accuracy of the above procedure for identifying signal sequences encoding signal peptides was evaluated by applying the method to the 43 amino terminal amino acids of all human SwissProt proteins. The computed Von Heijne score for each protein was compared with the known characterization of the protein as being a secreted protein or a non-secreted protein. In this manner, the number of non-secreted proteins having a score higher than 3.5 (false positives) and the number of secreted proteins having a score lower than 3.5 (false negatives) could be calculated.

Using the results of the above analysis, the probability that a peptide encoded by the 5' region of the mRNA is in fact a genuine signal peptide based on its Von Heijne's score was calculated based on either the assumption that 10% of human proteins are secreted or the assumption that 20% of human proteins are secreted. The results of this analysis are shown in Figures 2 and 3.

Using the above method of identifying secretory proteins, 5' ESTs for human glucagon, gamma interferon induced monokine precursor, secreted cyclophilin-like protein, human pleiotropin, and human biotinidase precursor all of which are polypeptides which are known to be secreted, were obtained. Thus, the above method successfully identified those 5' ESTs which encode a signal peptide. Prace:

To confirm that the signal peptide encoded by the 5' ESTs actually functions as a signal peptide, the signal sequences from the 5' ESTs may be closed/into a reactor designed for the identification of signal peptides. Some signal peptide identification vectors are designed to confirm the ability to grow in selective medium on host cells which have a signal sequence operably inserted into the vectors For example, to confirm that a 5' EST encodes a genuine signal peptide, the signal sequence of the 5' EST may be inserted upstream and in frame with a non-secreted form of the yeast invertase gene in signal peptide selection vectors such as those described in U.S. Patent No. 5,536,637. Growth of host cells containing signal sequence selection vectors having the signal sequence from the 5' EST inserted therein confirms that the 5' EST encodes a genuine signal peptide.

Alternatively, the presence of a signal peptide may be confirmed by cloning the extended cDNAs obtained using the ESTs into expression vectors such as pXT1 (as described below), or by constructing promoter-signal sequence-reporter gene vectors which encode fusion proteins between the signal peptide and an assayable reporter protein. After introduction of these vectors into a suitable host cell, such as COS cells or NIH 3T3 cells, the growth medium may be harvested and analyzed for the presence of the secreted protein. The medium from these cells is compared to the medium from cells containing vectors lacking the signal sequence or extended cDNA insert to identify vectors which encode a functional signal peptide or an authentic secreted protein.

Those 5' ESTs which encoded a signal peptide, as determined by the method of Example 22 above, were further grouped into four categories based on their homology to known sequences. The categorization of the 5' ESTs is described in Example 24 below.

EXAMPLE 24

Categorization of 5' ESTs Encoding a Signal Peptide

Those 5' ESTs having a sequence not matching any known vertebrate sequence nor any publicly available EST sequence were designated "new." Of the sequences in the SIGNALTAG™ database, 947 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

5 Those 5' ESTs having a sequence not matching any vertebrate sequence but matching a publicly known EST were designated "EST-ext", provided that the known EST sequence was extended by at least 40 nucleotides in the 5' direction. Of the sequences in the SIGNALTAG™ database, 150 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those ESTs not matching any vertebrate sequence but matching a publicly known EST without extending the 10 known EST by at least 40 nucleotides in the 5' direction were designated "EST." Of the sequences in the SIGNALTAG™ database, 599 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those 5' ESTs matching a human mRNA sequence but extending the known sequence by at least 40 nucleotides in the 5' direction were designated "VERT-ext." Of the sequences in the SIGNALTAGTM database, 23 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category. Included in this category was a 5' EST which 15 extended the known sequence of the human translocase mRNA by more than 200 bases in the 5' direction. A 5' EST which extended the sequence of a human tumor suppressor gene in the 5' direction was also identified.

Figure 4 shows the distribution of 5' ESTs in each category and the number of 5' ESTs in each category having a given minimum von Heijne's score.

Each of the 5' ESTs was categorized based on the tissue from which its corresponding mRNA was obtained, 20 as described below in Example 25.

EXAMPLE 25

Categorization of Expression Patterns

Figure 5 shows the tissues from which the mRNAs corresponding to the 5' ESTs in each of the above described categories were obtained.

In addition to categorizing the 5' ESTs by the tissue from which the cDNA library in which they were first identified was obtained, the spatial and temporal expression patterns of the mRNAs corresponding to the 5' ESTs, as well as their expression levels, may be determined as described in Example 26 below. Characterization of the spatial and temporal expression patterns and expression levels of these mRNAs is useful for constructing expression vectors capable of producing a desired level of gene product in a desired spatial or temporal manner, as will be discussed in more detail 30 below.

In addition, 5' ESTs whose corresponding mRNAs are associated with disease states may also be identified. For example, a particular disease may result from lack of expression, over expression, or under expression of an mRNA corresponding to a 5' EST. By comparing mRNA expression patterns and quantities in samples taken from healthy

individuals with those from individuals suffering from a particular disease, 5' ESTs responsible for the disease may be identified.

It will be appreciated that the results of the above characterization procedures for 5' ESTs also apply to extended cDNAs (obtainable as described below) which contain sequences adjacent to the 5' ESTs. It will also be appreciated that if it is desired to defer characterization until extended cDNAs have been obtained rather than characterizing the ESTs themselves, the above characterization procedures can be applied to characterize the extended cDNAs after their isolation.

EXAMPLE 26

Evaluation of Expression Levels and Patterns of mRNAs Corresponding to 5' ESTs or Extended cDNAs

10

Expression levels and patterns of mRNAs corresponding to 5' ESTs or extended cDNAs (obtainable as described below) may be analyzed by solution hybridization with long probes as described in International Patent Application No. WO 97/05277. Briefly, a 5' EST, extended cDNA, or fragment thereof corresponding to the gane encoding the mRNA to be characterized is inserted at a cloning site immediately downstream of a bacteriophage (T3, T7 or SP6) RNA polymerase promoter to produce antisense RNA. Preferably, the 5' EST or extended cDNA has 100 or more nucleotides. The plasmid is linearized and transcribed in the presence of ribonucleotides comprising modified ribonucleotides (i.e. biotin-UTP and DIG-UTP). An excess of this doubly labeled RNA is hybridized in solution with mRNA isolated from cells or tissues of interest. The hybridizations are performed under standard stringent conditions (40-50°C for 16 hours in an 80% formamide, 0.4 M NaCl buffer, pH 7-8). The unhybridized probe is removed by digestion with ribonucleases specific for single-stranded RNA (i.e. RNases CL3, T1, Phy M, U2 or A). The presence of the biotin-UTP modification enables capture of the hybrid on a microtitration plate coated with streptavidin. The presence of the DIG modification enables the hybrid to be detected and quantified by ELISA using an anti-DIG antibody coupled to alkaline phosphatase.

The 5' ESTs, extended cDNAs, or fragments thereof may also be tagged with nucleotide sequences for the serial analysis of gene expression (SAGE) as disclosed in UK Patent Application No. 2 305 241 A. In this method, cDNAs are prepared from a cell, tissue, organism or other source of nucleic acid for which it is desired to determine gene expression patterns. The resulting cDNAs are separated into two pools. The cDNAs in each pool are cleaved with a first restriction endonuclease, called an "anchoring enzyme," having a recognition site which is likely to be present at least once in most cDNAs. The fragments which contain the 5' or 3' most region of the cleaved cDNA are isolated by binding to a capture medium such as streptavidin coated beads. A first oligonucleotide linker having a first sequence for hybridization of an amplification primer and an internal restriction site for a "tagging endonuclease" is ligated to the digested cDNAs in the first pool. Digestion with the second endonuclease produces short "tag" fragments from the cDNAs.

25

A second oligonucleotide having a second sequence for hybridization of an amplification primer and an internal restriction site is ligated to the digested cDNAs in the second pool. The cDNA fragments in the second pool are also digested with the "tagging endonuclease" to generate short "tag" fragments derived from the cDNAs in the second pool. The "tags" resulting from digestion of the first and second pools with the anchoring enzyme and the tagging 5 endonuclease are ligated to one another to produce "ditags." In some embodiments, the ditags are concatamerized to produce ligation products containing from 2 to 200 ditags. The tag sequences are then determined and compared to the sequences of the 5' ESTs or extended cDNAs to determine which 5' ESTs or extended cDNAs are expressed in the cell, tissue, organism, or other source of nucleic acids from which the tags were derived. In this way, the expression pattern of the 5' ESTs or extended cDNAs in the cell, tissue, organism, or other source of nucleic acids is obtained.

Quantitative analysis of gene expression may also be performed using arrays. As used herein, the term array means a one dimensional, two dimensional, or multidimensional arrangement of full length cDNAs (i.e. extended cDNAs which include the coding sequence for the signal peptide, the coding sequence for the mature protein, and a stop codon), extended cDNAs, 5' ESTs or fragments of the full length cDNAs, extended cDNAs, or 5' ESTs of sufficient length to permit specific detection of gene expression. Preferably, the fragments are at least 15 nucleotides in length. More 15 preferably, the fragments are at least 100 nucleotides in length. More preferably, the fragments are more than 100 nucleotides in length. In some embodiments the fragments may be more than 500 nucleotides in length.

For example, quantitative analysis of gene expression may be performed with full length cDNAs, extended cDNAs, 5' ESTs, or fragments thereof in a complementary DNA microarray as described by Schena et al. (Science 270:467-470, 1995; Proc. Natl. Acad. Sci. U.S.A. 93:10614-10619, 1996). Full length cDNAs, extended cDNAs, 5' 20 ESTs or fragments thereof are amplified by PCR and arrayed from 96-well microtiter plates anto silvlated microscope stides using high-speed robotics. Printed arrays are incubated in a humid chamber to allow rehydration of the array elements and rinsed, once in 0.2% SDS for 1 min, twice in water for 1 min and once for 5 min in sodium borohydride solution. The arrays are submerged in water for 2 min at 95°C, transferred into 0.2% SDS for 1 min, rinsed twice with water, air dried and stored in the dark at 25°C.

Cell or tissue mRNA is isolated or commercially obtained and probes are prepared by a single round of reverse transcription. Probes are hybridized to 1 cm² microarrays under a 14 x 14 mm glass coverslip for 6-12 hours at 60°C. Arrays are washed for 5 min at 25°C in low stringency wash buffer (1 x SSC/0.2% SDS), then for 10 min at room temperature in high stringency wash buffer (0.1 x SSC/0.2% SDS). Arrays are scanned in 0.1 x SSC using a fluorescence laser scanning device fitted with a custom filter set. Accurate differential expression measurements are 30 obtained by taking the average of the ratios of two independent hypridizations.

Quantitative analysis of the expression of genes may also be performed with full length cDNAs, extended cDNAs, 5' ESTs, or fragments thereof in complementary DNA arrays as described by Pietu et al. (Genome Research 6:492-503, 1996). The full length cDNAs, extended cDNAs, 5' ESTs or tragments thereof are PCR amplified and spotted on membranes. Then, mRNAs originating from various tissues or cells are labeled with radioactive nucleotides. WO 99/31236 PCT/IB98/02122

-31-

After hybridization and washing in controlled conditions, the hybridized mRNAs are detected by phospho-imaging or autoradiography. Duplicate experiments are performed and a quantitative analysis of differentially expressed mRNAs is then performed.

Alternatively, expression analysis of the 5' ESTs or extended cDNAs can be done through high density

nucleotide arrays as described by Lockhart et al. (Nature Biotechnology 14: 1675-1680, 1996) and Sosnowsky et al.

(Proc. Natl. Acad. Sci. 94:1119-1123, 1997). Oligonucleotides of 15-50 nucleotides corresponding to sequences of the

5' ESTs or extended cDNAs are synthesized directly on the chip (Lockhart et al., supre) or synthesized and then

addressed to the chip (Sosnowski et al., supre). Preferably, the oligonucleotides are about 20 nucleotides in length.

cDNA probes labeled with an appropriate compound, such as biotin, digoxigenin or fluorescent dye, are

synthesized from the appropriate mRNA population and then randomly fragmented to an average size of 50 to 100 nucleotides. The said probes are then hybridized to the chip. After washing as described in Lockhart et al., supra and application of different electric fields (Sosnowsky et al., Proc. Natl. Acad. Sci. 94:1119-1123)., the dyes or labeling compounds are detected and quantified. Duplicate hybridizations are performed. Comparative analysis of the intensity of the signal originating from cDNA probes on the same target oligonucleotide in different cDNA samples indicates a differential expression of the mRNA corresponding to the 5' EST or extended cDNA from which the oligonucleotide sequence has been designed.

III. Use of 5' ESTs to Clone Extended cDNAs and to Clone the Corresponding Genomic DNAs

Once 5' ESTs which include the 5' end of the corresponding mRNAs have been selected using the procedures described above, they can be utilized to isolate extended cDNAs which contain sequences adjacent to the 5' ESTs. The extended cDNAs may include the entire coding sequence of the protein encoded by the corresponding mRNA, including the authentic translation start site, the signal sequence, and the sequence encoding the mature protein remaining after cleavage of the signal peptide. Such extended cDNAs are referred to herein as "full length cDNAs." Alternatively, the extended cDNAs may include only the sequence encoding the mature protein remaining after cleavage of the signal peptide, or only the sequence encoding the signal peptide.

Example 27 below describes a general method for obtaining extended cDNAs. Example 28 below describes the cloning and sequencing of several extended cDNAs, including extended cDNAs which include the entire coding sequence and authentic 5' end of the corresponding mRNA for several secreted proteins.

25

The methods of Examples 27, 28, and 29 can also be used to obtain extended cDNAs which encode less than the entire coding sequence of the secreted proteins encoded by the genes corresponding to the 5' ESTs. In some embodiments, the extended cDNAs isolated using these methods encode at least 10 amino acids of one of the proteins encoded by the sequences of SEQ ID NOs: 40-140 and 242-377. In further embodiments, the extended cDNAs encode at least 20 amino acids of the proteins encoded by the sequences of SEQ ID NOs: 40-140 and 242-377. In further embodiments, the extended cDNAs encode at least 30 amino acids of the sequences of SEQ ID NOs: 40-140 and

242-377. In a preferred embodiment, the extended cDNAs encode a full length protein sequence, which includes the protein coding sequences of SEO ID NOs: 40-140 and 242-377.

EXAMPLE 27

General Method for Using 5' ESTs to Clone and Sequence Extended cDNAs

The following general method has been used to quickly and efficiently isolate extended cDNAs including sequence adjacent to the sequences of the 5' ESTs used to obtain them. This method may be applied to obtain extended cDNAs for any 5' EST in the NETGENETM database, including those 5' ESTs encoding secreted proteins. The method is summarized in Figure 6.

1. Obtaining Extended cDNAs

10 a) First strand synthesis

The method takes advantage of the known 5' sequence of the mRNA. A reverse transcription reaction is conducted on purified mRNA with a poly 14dT primer containing a 49 nucleotide sequence at its 5' end allowing the addition of a known sequence at the end of the cDNA which corresponds to the 3' end of the mRNA. For example, the primer may have the following sequence: 5'-ATC GTT GAG ACT CGT ACC AGC AGA GTC ACG AGA GAG ACT ACA CGG TAC TGG TTT TTT TTT TTT TTVN -3' (SEQ ID NO:14). Those skilled in the art will appreciate that other sequences may also be added to the poly dT sequence and used to prime the first strand synthesis. Using this primer and a reverse transcriptase such as the Superscript II (Gibco BRL) or Rnase H Minus M-MLV/(Promega) enzyme, a reverse transcript anchored at the 3' polyA site of the RNAs is generated.

After removal of the mRNA hybridized to the first cDNA strand by alkaline hydrolysis, the products of the alkaline hydrolysis and the residual poly dT primer are eliminated with an exclusion column such as an AcA34 (Biosepra) matrix as explained in Example 11.

b) Second strand synthesis

30

A pair of nested primers on each end is designed based on the known 5' sequence from the 5' EST and the known 3' end added by the poly dT primer used in the first strand synthesis. Software used to design primers are either based on GC content and melting temperatures of oligonucleotides, such as OSP (Illier and Green, PCR Meth. Appl. 1:124-128, 1991), or based on the octamer frequency disparity method (Griffais et al., Nucleic Acids Res. 19: 3887-3891, 1991 such as PC-Rare (http://bioinformatics.weizmann.ac.il/software/PC-Rare/doc/manuel.html).

Preferably, the nested primers at the 5' end are separated from one another by four to nine bases. The 5' primer sequences may be selected to have melting temperatures and specificities suitable for use in PCR.

Preferably, the nested primers at the 3' end are separated from one another by four to nine bases. For example, the nested 3' primers may have the following sequences: (5' CCA GCA GAG TCA CGA GAG AGA CTA CAC GG -3'(SEQ ID NO:15), and 5'-CAC GAG AGA GAC TAC ACG GTA CTG G 3' (SEQ ID NO:16). These primers were selected because they have melting temperatures and specificities compatible with their use in PCR. However, those skilled in the art will appreciate that other sequences may also be used as primers.

The first PCR run of 25 cycles is performed using the Advantage Tth Polymerase Mix (Clontech) and the outer primer from each of the nested pairs. A second 20 cycle PCR using the same enzyme and the inner primer from each of the nested pairs is then performed on 1/2500 of the first PCR product. Thereafter, the primers and nucleotides are removed.

5 2. Sequencing of Full Length Extended cDNAs or Fragments Thereof

Due to the lack of position constraints on the design of 5' nested primers compatible for PCR use using the OSP software, amplicons of two types are obtained. Preferably, the second 5' primer is located upstream of the translation initiation codon thus yielding a nested PCR product containing the whole coding sequence. Such a full length extended cDNA undergoes a direct cloning procedure as described in section a below. However, in some cases, the second 5' primer is located downstream of the translation initiation codon, thereby yielding a PCR product containing only part of the ORF. Such incomplete PCR products are submitted to a modified procedure described in section b below.

a) Nested PCR products containing complete ORFs

When the resulting nested PCR product contains the complete coding sequence, as predicted from the 5'EST sequence, it is cloned in an appropriate vector such as pED6dpc2, as described in section 3.

b) Nested PCR products containing incomplete ORFs

When the amplicon does not contain the complete coding sequence, intermediate steps are necessary to obtain both the complete coding sequence and a PCR product containing the full coding sequence. The complete coding sequence can be assembled from several partial sequences determined directly from different PCR products as described in the following section.

Once the full coding sequence has been completely determined, new primers compatible for PCR use are designed to obtain amplicons containing the whole coding region. However, in such cases, 3' primers compatible for PCR use are located inside the 3' UTR of the corresponding mRNA, thus yielding amplicons which lack part of this region, i.e. the polyA tract and sometimes the polyadenylation signal, as illustrated in figure 6. Such full length extended cDNAs are then cloned into an appropriate vector as described in section 3.

c) Sequencing extended cDNAs

Sequencing of extended cDNAs is performed using a Die Terminator approach with the AmpliTaq DNA polymerase FS kit available from Perkin Elmer.

In order to sequence PCR fragments, primer walking is performed using software such as OSP to choose

30 primers and automated computer software such as ASMG (Sutton et al., Genome Science Technol. 1: 9-19, 1995) to construct contigs of walking sequences including the initial 5' tag using minimum overlaps of 32 nucleotides. Preferably, primer walking is performed until the sequences of full length cDNAs are obtained.

Completion of the sequencing of a given extended cDNA fragment is assessed as follows. Since sequences located after a polyA tract are difficult to determine precisely in the case of uncloned products, sequencing and primer

walking processes for PCR products are interrupted when a polyA tract is identified in extended cDNAs obtained as described in case b. The sequence length is compared to the size of the nested PCR product obtained as described above. Due to the limited accuracy of the determination of the PCR product size by gel electrophoresis, a sequence is considered complete if the size of the obtained sequence is at least 70 % the size of the first nested PCR product. If the length of the sequence determined from the computer analysis is not at least 70% of the length of the nested PCR product, these PCR products are cloned and the sequence of the insertion is determined. When Northern blot data are available, the size of the mRNA detected for a given PCR product is used to finally assess that the sequence is complete. Sequences which do not fulfill the above criteria are discarded and will undergo a new isolation procedure.

Sequence data of all extended cDNAs are then transferred to a proprietary database, where quality controls and validation steps are carried out as described in example 15.

3. Cloning of Full Length Extended cDNAs

The PCR product containing the full coding sequence is then cloned in an appropriate vector. For example, the extended cDNAs can be cloned into the expression vector pED6dpc2 (DiscoverEase, Genetics Institute, Cambridge, MA) as follows. The structure of pED6dpc2 is shown in Figure 7. pED6dpc2 vector DNA is prepared with blunt ends by performing an EcoRI digestion followed by a fill in reaction. The blunt ended vector is dephosphorylated. After removal of PCR primers and ethanol precipitation, the PCR product containing the full coding sequence or the extended cDNA obtained as described above is phosphorylated with a kinase subsequently removed by phenol-Sevag extraction and precipitation. The double stranded extended cDNA is then ligated to the vector and the resulting expression plasmid introduced into appropriate host cells.

Since the PCR products obtained as described above are blunt ended molecules that can be cloned in either direction, the orientation of several clones for each PCR product is determined. Then, 4 to 10 clones are ordered in microtiter plates and subjected to a PCR reaction using a first primer located in the vector close to the cloning site and a second primer located in the portion of the extended cDNA corresponding to the 3' end of the mRNA. This second primer may be the antisense primer used in anchored PCR in the case of direct cloning (case a) or the antisense primer located inside the 3'UTR in the case of indirect cloning (case b). Clones in which the start codon of the extended cDNA is operably linked to the promoter in the vector so as to permit expression of the protein encoded by the extended cDNA are conserved and sequenced. In addition to the ends of cDNA inserts, approximately 50 bp of vector DNA on each side of the cDNA insert are also sequenced.

The cloned PCR products are then entirely sequenced according to the aforementioned procedure. In this case, contig assembly of long fragments is then performed on walking sequences that have already contigated for uncloned PCR products during primer walking. Sequencing of cloned amplicons is complete when the resulting contigs include the whole coding region as well as overlapping sequences with vector DNA on both ends.

4. Computer Analysis of Full Length Extended cDNA

.35-

Sequences of all full length extended cDNAs are then submitted to further analysis as described below and using the parameters found in Table II with the following modifications. For screening of miscellaneous subdivisions of Genbank, FASTA was used instead of BLASTN and 15 nucleotide of homology was the limit instead of 17. For Alu detection, BLASTN was used with the following parameters: S = 72; identity = 70%; and length = 40 nucleotides.

- Polyadenylation signal and polyA tail which were not search for the 5' ESTs were searched. For polyadenylation signal detection the signal (AATAAA) was searched with one permissible mismatch in the last ten nucleotides preceding the 5' end of the polyA. For the polyA, a stretch of 8 amino acids in the last 20 nucleotides of the sequence was searched with BLAST2N in the sense strand with the following parameters (W = 6, S = 10, E = 1000, and identity = 90%). Finally, patented sequences and ORF homologies were searched using, respectively, BLASTN and BLASTP on GenSEQ
- 10 (Derwent's database of patented nucleotide sequences) and SWISSPROT for ORFs with the following parameters (W = 8 and B = 10). Before examining the extended full length cDNAs for sequences of interest, extended cDNAs which are not of interest are searched as follows.

a) Elimination of undesired sequences

Although 5'ESTs were checked to remove contaminant sequences as described in Example 18, a last verification was carried out to identify extended cDNAs sequences derived from undesired sequences such as vector RNAs, transfer RNAs, ribosomal rRNAs, mitochondrial RNAs, prokaryotic RNAs and fungal RNAs using the FASTA and BLASTN programs on both strands of extended cDNAs as described below.

To identify the extended cDNAs encoding vector RNAs, extended cDNAs are compared to the known sequences of vector RNA using the FASTA program. Sequences of extended cDNAs with more than 90% homology over stretches of 15 nucleotides are identified as vector RNA.

To identify the extended cDNAs encoding tRNAs, extended cDNA sequences were compared to the sequences of 1190 known tRNAs obtained from EMBL release 38, of which 100 were human. Sequences of extended cDNAs having more than 80% homology over 60 nucleotides using FASTA were identified as tRNA.

To identify the extended cDNAs encoding rRNAs, extended cDNA sequences were compared to the sequences
of 2497 known rRNAs obtained from EMBL release 38, of which 73 were human. Sequences of extended cDNAs having
more than 80% homology over stretches longer than 40 nucleotides using BLASTN were identified as rRNAs.

To identify the extended cDNAs encoding mtRNAs, extended cDNA sequences were compared to the sequences of the two known mitochondrial genomes for which the entire genomic sequences are available and all sequences transcribed from these mitochondrial genomes including tRNAs, rRNAs, and mRNAs for a total of 38 sequences. Sequences of extended cDNAs having more than 80% homology over stretches longer than 40 nucleotides using BLASTN were identified as mtRNAs.

Sequences which might have resulted from other exogenous contaminants were identified by comparing extended cDNA sequences to release 105 of Genbank bacterial and fungal divisions. Sequences of extended cDNAs

having more than 90% homology over 40 nucleotides using BLASTN were identified as exogenous prokaryotic or fungal contaminants.

In addition, extended cDNAs were searched for different repeat sequences, including Alu sequences, L1 sequences, THE and MER repeats, SSTR sequences or satellite, micro-satellite, or telomeric repeats. Sequences of extended cDNAs with more than 70% homology over 40 nucleotide stretches using BLASTN were identified as repeat sequences and masked in further identification procedures. In addition, clones showing extensive homology to repeats, i.e., matches of either more than 50 nucleotides if the homology was at least 75% or more than 40 nucleotides if the homology was at least 90%, were flagged.

b) Identification of structural features

10

Structural features, e.g. polyA tail and polyadenylation signal, of the sequences of full length extended cDNAs are subsequently determined as follows.

A polyA tail is defined as a homopolymeric stretch of at least 11 A with at most one alternative base within it.

The polyA tail search is restricted to the last 20 nt of the sequence and limited to stretches of 11 consecutive A's because sequencing reactions are often not readable after such a polyA stretch. Stretches with 100% homology over 6 nucleotides are identified as polyA tails.

To search for a polyadenylation signal, the polyA tail is clipped from the full-length sequence. The 50 bp preceding the polyA tail are searched for the canonic polyadenylation AAUAAA signal allowing one mismatch to account for possible sequencing errors and known variation in the canonical sequence of the polyadenylation signal.

c) Identification of functional features

20 _ Functional features, e.g. ORFs and signal sequences, of the sequences of full length extended cDNAs were subsequently determined as follows.

The 3 upper strand frames of extended cDNAs are searched for ORFs defined as the maximum length fragments beginning with a translation initiation codon and ending with a stop codon. ORFs encoding at least 20 amino acids are preferred.

Each found ORF is then scanned for the presence of a signal peptide in the first 50 amino-acids or, where appropriate, within shorter regions down to 20 amino acids or less in the ORF, using the matrix method of von Heijne (Nuc. Acids Res. 14: 4683-4690 (1986)) and the modification described in Example 22.

d) Homology to either nucleotidic or proteic sequences

Sequences of full length extended cDNAs are then compared to known sequences on a nucleotidic or proteic 30 basis.

Sequences of full length extended cDNAs are compared to the following known nucleic acid sequences: vertebrate sequences (Genbank), EST sequences (Genbank), patented sequences (Geneseqn) and recently identified sequences (Genbank daily releases) available at the time of filing for the priority documents. Full length cDNA sequences are also compared to the sequences of a private database (Genset internal sequences) in order to find sequences that

have already been identified by applicants. Sequences of full length extended cDNAs with more than 90% homology over 30 nucleotides using either BLASTN or BLAST2N as indicated in Table III are identified as sequences that have already been described. Matching vertebrate sequences are subsequently examined using FASTA; full length extended cDNAs with more than 70% homology over 30 nucleotides are identified as sequences that have already been described.

ORFs encoded by full length extended cDNAs as defined in section c) are subsequently compared to known amino acid sequences found in Swissprot release CHP, PIR release PIR# and Genpept release GPEPT public databases using BLASTP with the parameter W = 8 and allowing a maximum of 10 matches. Sequences of full length extended cDNAs showing extensive homology to known protein sequences are recognized as already identified proteins.

In addition, the three-frame conceptual translation products of the top strand of full length extended cDNAs

are compared to publicly known amino acid sequences of Swissprot using BLASTX with the parameter E = 0.001.

Sequences of full length extended cDNAs with more than 70% homology over 30 amino acid stretches are detected as already identified proteins.

5. Selection of Cloned Full Length Sequences of the Present Invention

Cloned full length extended cDNA sequences that have already been characterized by the aforementioned computer analysis are then submitted to an automatic procedure in order to preselect full length extended cDNAs containing sequences of interest.

a) Automatic sequence preselection

All complete cloned full length extended cDNAs clipped for vector on both ends are considered. First, a negative selection is operated in order to eliminate unwanted cloned sequences resulting from either contaminants or PCR artifacts as follows. Sequences matching contaminant sequences such as vector RNA, tRNA, mtRNA, rRNA sequences are discarded as well as those encoding ORF sequences exhibiting extensive homology to repeats as defined in section 4 a). Sequences obtained by direct cloning using nested primers on 5' and 3' tags (section 1, case a) but lacking polyA tail are discarded. Only ORFs containing a signal peptide and ending either before the polyA tail (case a) or before the end of the cloned 3'UTR (case b) are kept. Then, ORFs containing unlikely mature proteins such as mature proteins which size is less than 20 amino acids or less than 25% of the immature protein size are eliminated.

In the selection of the OFR, priority was given to the ORF and the frame corresponding to the polypeptides described in SignalTag Patents (United States Patent Application Serial Nos: 08/905,223; 08/905,135; 08/905,051; 08/905,144; 08/905,279; 08/904,468; 08/905,134; and 08/905,133). If the ORF was not found among the OFRs described in the SignalTag Patents, the ORF encoding the signal peptide with the highest score according to Von Heijne method as defined in Example 22 was chosen. If the scores were identical, then the longest ORF was chosen.

Sequences of full length extended cDNA clones are then compared pairwise with BLAST after masking of the repeat sequences. Sequences containing at least 90% homology over 30 nucleotides are clustered in the same class. Each cluster is then subjected to a cluster analysis that detects sequences resulting from internal priming or from

alternative splicing, identical sequences or sequences with several frameshifts. This automatic analysis serves as a basis for manual selection of the sequences.

b) Manual sequence selection

Manual selection is carried out using automatically generated reports for each sequenced full length extended cDNA clone. During this manual procedures, a selection is operated between clones belonging to the same class as follows. ORF sequences encoded by clones belonging to the same class are aligned and compared. If the homology between nucleotidic sequences of clones belonging to the same class is more than 90% over 30 nucleotide stretches or if the homology between amino acid sequences of clones belonging to the same class is more than 80% over 20 amino acid stretches, than the clones are considered as being identical. The chosen ORF is the best one according to the criteria mentioned below. If the nucleotide and amino acid homologies are less than 90% and 80% respectively, the clones are said to encode distinct proteins which can be both selected if they contain sequences of interest.

Selection of full length extended cDNA clones encoding sequences of interest is performed using the following criteria. Structural parameters (initial tag, polyadenylation site and signal) are first checked. Then, homologies with known nucleic acids and proteins are examined in order to determine whether the clone sequence match a known nucleic/proteic sequence and, in the latter case, its covering rate and the date at which the sequence became public. If there is no extensive match with sequences other than ESTs or genomic DNA, or if the clone sequence brings substantial new information, such as encoding a protein resulting from alternative slicing of an mRNA coding for an already known protein, the sequence is kept. Examples of such cloned full length extended cDNAs containing sequences of interest are described in Example 28. Sequences resulting from chimera or double inserts as assessed by homology to other sequences are discarded during this procedure.

EXAMPLE 28

Cloning and Sequencing of Extended cDNAs

The procedure described in Example 27 above was used to obtain the extended cDNAs of the present invention. Using this approach, the full length cDNA of SEQ ID NO:17 was obtained. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MKKVLLLITAILAVAVG (SEQ ID NO: 18) having a von Heijne score of 8.2.

The full length cDNA of SEQ ID NO:19 was also obtained using this procedure. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MWWFQQGLSFLPSALVIWTSA (SEQ ID NO:20) having a von Heijne score of 5.5.

Another full length cDNA obtained using the procedure described above has the sequence of SEQ ID NO:21.

This cDNA, falls into the "EST-ext" category described above and encodes the signal peptide

MVLTTLPSANSANSPVNMPTTGPNSLSYASSALSPCLT (SEQ ID NO:22) having a von Heijne score of 5.9.

WO 99/31236

10

30

The above procedure was also used to obtain a full length cDNA having the sequence of SEQ ID NO:23. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide ILSTVTALTFAXA (SEQ ID NO:24) having a von Heijne score of 5.5.

The full length cDNA of SEQ ID NO:25 was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal paptide LVLTLCTLPLAVA (SEQ ID NO:26) having a von Heijne score of 10.1.

The full length cDNA of SEQ ID NO:27 was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal peptide LWLLFFLVTAIHA (SEQ ID NO:28) having a von Heijne score of 10.7.

The above procedures were also used to obtain the extended cDNAs of the present invention. 5' ESTs expressed in a variety of tissues were obtained as described above. The appended sequence listing provides the tissues from which the extended cDNAs were obtained. It will be appreciated that the extended cDNAs may also be expressed in tissues other than the tissue listed in the sequence listing.

5' ESTs obtained as described above were used to obtain extended cDNAs having the sequences of SEQ ID

NOs: 40-140 and 242-377. Table IV provides the sequence identification numbers of the extended cDNAs of the present invention, the locations of the full coding sequences in SEQ ID NOs: 40-140 and 242-377 (i.e. the nucleotides encoding both the signal peptide and the mature protein, listed under the heading FCS location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the signal peptides (listed under the heading SigPep Location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the mature proteins generated by cleavage of the signal peptides (listed under the heading Mature Polypeptide Location in Table IV), the locations in SEQ ID NOs: 40-140 and 242-377 of stop codons (listed under the heading Stop Codon Location in Table IV), the locations in SEQ ID NOs: 40-140 and 242-377 of polyA signals (listed under the heading Poly A Signal Location in Table IV) and the locations of polyA sites (listed under the heading Poly A Site Location in Table IV).

The polypeptides encoded by the extended cDNAs were screened for the presence of known structural or

functional motifs or for the presence of signatures, small amino acid sequences which are well conserved amongst the
members of a protein family. The conserved regions have been used to derive consensus patterns or matrices included in
the PROSITE data bank, in particular in the file prosite.dat (Release 13.0 of November 1995, located at
http://expasy.hcuge.ch/sprot/prosite.html. Prosite_convert and prosite_scan programs
(http://ulrec3.unil.ch/ftpserveur/prosite_scan) were used to find signatures on the extended cDNAs.

For each pattern obtained with the prosite_convert program from the prosite.dat file, the accuracy of the detection on a new protein sequence has been tested by evaluating the frequency of irrelevant hits on the population of human secreted proteins included in the data bank SWISSPROT. The ratio between the number of hits on shuffled proteins (with a window size of 20 amino acids) and the number of hits on native (unshuffled) proteins was used as an index. Every pattern for which the ration was greater than 20% (one hit on shuffled proteins for 5 hits on native

proteins) was skipped during the search with prosite_scan. The program used to shuffle protein sequences (db_shuffled) and the program used to determine the statistics for each pattern in the protein data banks (prosite_statistics) are available on the ftp site http://ulrec3.unil.ch/ftpserveur/prosite_scan.

Table V lists the sequence identification numbers of the polypeptides of SEQ ID NOs: 141-241 and 378-513, the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the full length polypeptide (second column), the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the signal peptides (third column), and the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the mature polypeptide created by cleaving the signal peptide from the full length polypeptide (fourth column).

The nucleotide sequences of the sequences of SEQ ID NOs: 40-140 and 242-377 and the amino acid sequences of SEQ ID NOs: 141-241 and 378-513) are provided in the appended sequence listing. In some instances, the sequences are preliminary and may include some incorrect or ambiguous sequences or amino acids. The sequences of SEQ ID NOs: 40-140 and 242-377 can readily be screened for any errors therein and any sequence ambiguities can be resolved by resequencing a fragment containing such errors or ambiguities on both strands. Nucleic acid fragments for resolving sequencing errors or ambiguities may be obtained from the deposited clones or can be isolated using the techniques described herein. Resolution of any such ambiguities or errors may be facilitated by using primers which hybridize to sequences located close to the ambiguous or erroneous sequences. For example, the primers may hybridize to sequences within 50-75 bases of the ambiguity or error. Upon resolution of an error or ambiguity, the corresponding corrections can be made in the protein sequences encoded by the DNA containing the error or ambiguity. For example, in the sequences of the present invention, ambiguities in the sequence of SEQ ID NO: 131 were resolved. The amino acid sequence of the protein encoded by a particular clone can also be determined by expression of the clone in a suitable host cell, collecting the protein, and determining its sequence.

For each amino acid sequence, Applicants have identified-what they have determined to be the reading frame best identifiable with sequence information available at the time of filing. Some of the amino acid sequences may contain "Xaa" designators. These "Xaa" designators indicate either (1) a residue which cannot be identified because of nucleotide sequence ambiguity or (2) a stop codon in the determined sequence where Applicants believe one should not exist (if the sequence were determined more accurately).

Cells containing the extended cDNAs (SEQ ID NOs: 40-140 and 242-377) of the present invention in the vector pED6dpc2, are maintained in permanent deposit by the inventors at Genset, S.A., 24 Rue Royale, 75008 Paris, France.

Pools of cells containing the extended cDNAs (SEQ ID NOs: 40-140 and 242-377), from which cells containing a particular polynucleotide are obtainable, were deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209 or the European Collection of Cell Cultures, Vaccine Research and Production Laboratory, Public Health Laboratory Service, Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire SP4 0JG, United Kingdom. Each extended cDNA clone has been transfected into separate bacterial cells (E-

coli) for this composite deposit. Table VI lists the deposit numbers of the clones containing the extended cDNAs of the present invention. Table VII provides the internal designation number assigned to each SEQ ID NO and indicates whether the sequence is a nucleic acid sequence or a protein sequence.

Each extended cDNA can be removed from the pED6dpc2 vector in which it was deposited by performing a

Notl, Pstl double digestion to produce the appropriate fragment for each clone. The proteins encoded by the extended cDNAs may also be expressed from the promoter in pED6dpc2.

Bacterial cells containing a particular clone can be obtained from the composite deposit as follows:

An oligonucleotide probe or probes should be designed to the sequence that is known for that particular clone.

This sequence can be derived from the sequences provided herein, or from a combination of those sequences. The design of the oligonucleotide probe should preferably follow these parameters:

- (a) It should be designed to an area of the sequence which has the fewest ambiguous bases ("N's"), if any;
- (b) Preferably, the probe is designed to have a T_m of approx. 80°C (assuming 2 degrees for each A or T and 4 degrees for each G or C). However, probes having melting temperatures between 40 °C and 80 °C may also be used provided that specificity is not lost.
- The oligonucleotide should preferably be labeled with (-[32P]ATP (specific activity 6000 Cilmmole) and T4 polynucleotide kinase using commonly employed techniques for labeling oligonucleotides. Other labeling techniques can also be used. Unincorporated label should preferably be removed by gel filtration chromatography or other established methods. The amount of radioactivity incorporated into the probe should be quantified by measurement in a scintillation counter. Preferably, specific activity of the resulting probe should be approximately 4X10⁶ dpm/pmole.
- The bacterial culture containing the pool of full-length clones should preferably be thawed and 100 µl of the stock used to inoculate a sterile culture flask containing 25 ml of sterile L-broth containing ampicillin at 100 µg/ml. The culture should preferably be grown to saturation at 37°C, and the saturated culture should preferably be diluted in fresh L-broth. Aliquots of these dilutions should preferably be plated to determine the dilution and volume which will yield approximately 5000 distinct and well-separated colonies on solid bacteriological media containing L-broth containing approximately 5000 distinct and against 1.5% in a 150 mm petri dish when grown overnight at 37°C. Other known methods of obtaining distinct, well-separated colonies can also be employed.

Standard colony hybridization procedures should then be used to transfer the colonies to nitrocellulose filters and lyse, denature and bake them.

The filter is then preferably incubated at 65°C for 1 hour with gentle agitation in 6X SSC (20X stock is 175.3 g NaC1/liter, 88.2 g Na citrate/liter, adjusted to pH 7.0 with NaOH) containing 0.5% SDS, 100 pg/ml of yeast RNA, and 10 mM EDTA (approximately 10 mL per 150 mm filter). Preferably, the probe is then added to the hybridization mix at a concentration greater than or equal to 1X10⁶ dpm/mL. The filter is then preferably incubated at 65°C with gentle agitation overnight. The filter is then preferably washed in 500 mL of 2X SSC/0.1% SDS at room temperature with gentle shaking for 15 minutes. A third wash with 0.1X SSC/0.5% SDS at 65°C for 30 minutes to

15

30

1 hour is optional. The filter is then preferably dried and subjected to autoradiography for sufficient time to visualize the positives on the X-ray film. Other known hybridization methods can also be employed.

The positive colonies are picked, grown in culture, and plasmid DNA isolated using standard procedures. The clones can then be verified by restriction analysis, hybridization analysis, or DNA sequencing.

The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the extended cDNA insertion. For example, a PCR reaction may be conducted using a primer having the sequence GGCCATACACTTGAGTGAC (SEQ ID NO:38) and a primer having the sequence ATATAGACAAACGCACACC (SEQ. ID. NO:39). The PCR product which corresponds to the extended cDNA can then be manipulated using standard cloning 10 techniques familiar to those skilled in the art.

In addition to PCR based methods for obtaining extended cDNAs, traditional hybridization based methods may also be employed. These methods may also be used to obtain the genomic DNAs which encode the mRNAs from which the 5' ESTs were derived, mRNAs corresponding to the extended cDNAs, or nucleic acids which are homologous to extended cDNAs or 5' ESTs. Example 29 below provides an example of such methods.

EXAMPLE 29

Methods for Obtaining Extended cDNAs or Nucleic Acids Homologous to Extended cDNAs or 5' ESTs

A full length cDNA library can be made using the strategies described in Examples 13, 14, 15, and 16 above by replacing the random nonamer used in Example 14 with an oligo-dT primer. For instance, the oligonucleotide of SEQ ID 20 N9:14 may be used.

Alternatively, a cDNA library or genomic DNA library may be obtained from a commercial source or made using techniques familiar to those skilled in the art. The library includes cDNAs which are derived from the mRNA corresponding to a 5' EST or which have homology to an extended cDNA or 5' EST. The cDNA library or genomic DNA library is hybridized to a detectable probe comprising at least 10 consecutive nucleotides from the 5' EST or extended 25 cDNA using conventional techniques. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises at least 20-30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises at least 30 nucleotides from the 5' EST or extended cDNA. In other embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the 5' EST or extended cDNA.

Techniques for identifying cDNA clones in a cDNA library which hybridize to a given probe sequence are disclosed in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989. The same techniques may be used to isolate genomic DNAs.

Briefly, cDNA or genomic DNA clones which hybridize to the detectable probe are identified and isolated for further manipulation as follows. A grobe comprising at least 10 consecutive nucleotides from the 5' EST or extended cDNA is labeled with a detectable label such as a radioisotope or a fluorescent molecule. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises 20-30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the 5' EST or extended cDNA.

Techniques for labeling the probe are well known and include phosphorylation with polynucleotide kinase, nick translation, in vitro transcription, and non-radioactive techniques. The cDNAs or genomic DNAs in the library are transferred to a nitrocellulose or nylon filter and denatured. After incubation of the filter with a blocking solution, the filter is contacted with the labeled probe and incubated for a sufficient amount of time for the probe to hybridize to cDNAs or genomic DNAs containing a sequence capable of hybridizing to the probe.

By varying the stringency of the hybridization conditions used to identify extended cDNAs or genomic DNAs which hybridize to the detectable probe, extended cDNAS having different levels of homology to the probe identified and isolated. To identify extended cDNAs or genomic DNAs having a high degree of homology to the probe sequence, the melting temperature of the probe may be calculated using the following formulas:

For probes between 14 and 70 nucleotides in length the melting temperature (Tm) is calculated using the formula: Tm=81.5+16.6(log [Na+])+0.41(fraction G+C)-(600/N) where N is the length of the probe.

If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation Tm=81.5+16.6(log [Na+])+0.41(fraction G+C)-(0.63% formamide)-(600/N) where N is 20 the length of the probe.

Prehybridization may be carried out in 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100µg denatured fragmented salmon sperm DNA or 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100µg denatured fragmented salmon sperm DNA, 50% formamide. The formulas for SSC and Denhardt's solutions are listed in Sambrook et al., supra.

Hybridization is conducted by adding the detectable probe to the prehybridization solutions listed above. Where the probe comprises double stranded DNA, it is denatured before addition to the hybridization solution. The filter is contacted with the hybridization solution for a sufficient period of time to allow the probe to hybridize to extended cDNAs or genomic DNAs containing sequences complementary thereto or homologous thereto. For probes over 200 nucleotides in length, the hybridization may be carried out at 15-25°C below the Tm. For shorter probes, such as oligonucleotide probes, the hybridization may be conducted at 15-25°C below the Tm. Preferably, for hybridizations in 6X SSC, the hybridization is conducted at approximately 68°C. Preferably, for hybridizations in 50% formamide containing solutions, the hybridization is conducted at approximately 42°C.

All of the foregoing hybridizations would be considered to be under "stringent" conditions. Following hybridization, the filter is washed in 2X SSC, 0.1% SDS at room temperature for 15 minutes. The filter is then washed

with 0.1X SSC, 0.5% SDS at room temperature for 30 minutes to 1 hour. Thereafter, the solution is washed at the hybridization temperature in 0.1X SSC, 0.5% SDS. A final wash is conducted in 0.1X SSC at room temperature.

Extended cDNAs, nucleic acids homologous to extended cDNAs or 5' ESTs, or genomic DNAs which have hybridized to the probe are identified by autoradiography or other conventional techniques.

The above procedure may be modified to identify extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs having decreasing levels of homology to the probe sequence. For example, to obtain extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs of decreasing homology to the detectable probe, less stringent conditions may be used. For example, the hybridization temperature may be decreased in increments of 5°C from 68°C to 42°C in a hybridization buffer having a Na+ concentration of approximately 1M. Following 10 hybridization, the filter may be washed with 2X SSC, 0.5% SDS at the temperature of hybridization. These conditions are considered to be "moderate" conditions above 50°C and "low" conditions below 50°C.

Alternatively, the hybridization may be carried out in buffers, such as 6X SSC, containing formamide at a temperature of 42°C. In this case, the concentration of formamide in the hybridization buffer may be reduced in 5% increments from 50% to 0% to identify clones having decreasing levels of homology to the grobe. Following 15 hybridization, the filter may be washed with 6X SSC, 0.5% SDS at 50°C. These conditions are considered to be "moderate" conditions above 25% formamide and "low" conditions below 25% formamide.

Extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs which have hybridized to the probe are identified by autoradiography.

If it is desired to obtain nucleic acids homologous to extended cDNAs, such as allelic variants thereof or nucleic 20 acids encoding proteins related to the proteins encoded by the extended cDNAs, the level of homology between the hybridized nucleic acid and the extended cDNA or 5' EST used as the probe may readily be determined. To determine the level of homology between the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived, the nucleotide sequences of the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived are compared. For example, using the above methods, nucleic acids having at least 95% nucleic acid 25 homology to the extended cDNA or 5'EST from which the probe was derived may be obtained and identified. Similarly, by using progressively less stringent hybridization conditions one can obtain and identify nucleic acids having at least 90%, at least 85%, at least 80% or at least 75% homology to the extended cDNA or 5'EST from which the probe was derived. The level of homology between the hybridized nucleic acid and the extended cDNA or 5' EST used as the probe may be further determined using BLAST2N; parameters may be adapted depending on the sequence length and degree of 30 homology studied. In such comparisons, the default parameters or the parameters listed in Tables II and III may be used.

To determine whether a clone encodes a protein having a given amount of homology to the protein encoded by the extended cDNA or 5' EST, the amino acid sequence encoded by the extended cDNA or 5' EST is compared to the amino acid sequence encoded by the hybridizing nucleic acid. Homology is determined to exist when an amino acid sequence in the extended cDNA or 5' EST is closely related to an amino acid sequence in the hybridizing nucleic acid. A

sequence is closely related when it is identical to that of the extended cDNA or 5' EST or when it contains one or more amino acid substitutions therein in which amino acids having similar characteristics have been substituted for one another. Using the above methods, one can obtain nucleic acids encoding proteins having at least 95%, at least 90%, at least 85%, at least 80% or at least 75% homology to the proteins encoded by the extended cDNA or 5'EST from which the probe was derived. Using the above methods and algorithms such as FASTA with parameters depending on the sequence length and degree of homology studied the level of homology may be determined. In determining the level of homology using FASTA, the default parameters or the parameters listed in Tables II or III may be used.

Alternatively, extended cDNAs may be prepared by obtaining mRNA from the tissue, cell, or organism of interest using mRNA preparation procedures utilizing poly A selection procedures or other techniques known to those skilled in the art. A first primer capable of hybridizing to the poly A tail of the mRNA is hybridized to the mRNA and a reverse transcription reaction is performed to generate a first cDNA strand.

The first cDNA strand is hybridized to a second primer containing at least 10 consecutive nucleotides of the sequences of the 5' EST for which an extended cDNA is desired. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the sequences of the 5' EST. More preferably, the primer comprises 20-30 consecutive nucleotides from the sequences of the 5' EST. In some embodiments, the primer comprises more than 30 nucleotides from the sequences of the 5' EST. If it is desired to obtain extended cDNAs containing the full protein coding sequence, including the authentic translation initiation site, the second primer used contains sequences located upstream of the translation initiation site. The second primer is extended to generate a second cDNA strand complementary to the first cDNA strand. Alternatively, RTPCR may be performed as described above using primers from both ends of the cDNA to be obtained.

Extended cDNAs containing 5' fragments of the mRNA may be prepared by contacting an mRNA comprising the sequence of the 5' EST for which an extended cDNA is desired with a primer comprising at least 10 consecutive nucleotides of the sequences complementary to the 5' EST, hybridizing the primer to the mRNAs, and reverse transcribing the hybridized primer to make a first cDNA strand from the mRNAs. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST. More preferably, the primer comprises 20-30 consecutive nucleotides from the 5' EST.

Thereafter, a second cDNA strand complementary to the first cDNA strand is synthesized. The second cDNA strand may be made by hybridizing a primer complementary to sequences in the first cDNA strand to the first cDNA strand and extending the primer to generate the second cDNA strand.

The double stranded extended cDNAs made using the methods described above are isolated and cloned. The extended cDNAs may be cloned into vectors such as plasmids or viral vectors capable of replicating in an appropriate host cell. For example, the host cell may be a bacterial, mammalian, avian, or insect cell.

30

Techniques for isolating mRNA, reverse transcribing a primer hybridized to mRNA to generate a first cDNA strand, extending a primer to make a second cDNA strand complementary to the first cDNA strand, isolating the double

stranded cDNA and cloning the double stranded cDNA are well known to those skilled in the art and are described in Current Protocols in Molecular Biology, John Wiley 503 Sons, Inc. 1997 and Sambrook et al. Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989.

Alternatively, kits for obtaining full length cDNAs, such as the GeneTrapper (Cat. No. 10356-020, Gibco, BRL),

may be used for obtaining full length cDNAs or extended cDNAs. In this approach, full length or extended cDNAs are
prepared from mRNA and cloned into double stranded phagemids. The cDNA library in the double stranded phagemids is
then rendered single stranded by treatment with an endonuclease, such as the Gene II product of the phage F1, and
Exonuclease III as described in the manual accompanying the GeneTrapper kit. A biotinylated oligonucleotide comprising
the sequence of a 5' EST, or a fragment containing at least 10 nucleotides thereof, is hybridized to the single stranded
phagemids. Preferably, the fragment comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST. In some procedures, the fragment
may comprise more than 30 consecutive nucleotides from the 5' EST. For example, the fragment may comprises at least
40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the 5' EST.

Hybrids between the biotinylated oligonucleotide and phagemids having inserts containing the 5' EST sequence are isolated by incubating the hybrids with streptavidin coated paramagnetic beads and retrieving the beads with a magnet. Thereafter, the resulting phagemids containing the 5' EST sequence are released from the beads and converted into double stranded DNA using a primer specific for the 5' EST sequence. The resulting double stranded DNA is transformed into bacteria. Extended cDNAs containing the 5' EST sequence are identified by colony PCR or colony hybridization.

A plurality of extended cDNAs containing full length protein coding sequences or sequences encoding only the mature protein remaining after the signal peptide is cleaved may be provided as cDNA libraries for subsequent evaluation of the encoded proteins or use in diagnostic assays as described below.

IV. Expression of Proteins Encoded by Extended cDNAs Isolated Using 5' ESTs

Extended cDNAs containing the full protein coding sequences of their corresponding mRNAs or portions
thereof, such as cDNAs encoding the mature protein, may be used to express the secreted proteins or portions thereof which they encode as described in Example 30 below. If desired, the extended cDNAs may contain the sequences encoding the signal peptide to facilitate secretion of the expressed protein. It will be appreciated that a plurality of extended cDNAs containing the full protein coding sequences or portions thereof may be simultaneously cloned into expression vectors to create an expression library for analysis of the encoded proteins as described below.

EXAMPLE 30

Expression of the Proteins Encoded by Extended cDNAs or Portions Thereof

To express the proteins encoded by the extended cDNAs or portions thereof, nucleic acids containing the coding sequence for the proteins or portions thereof to be expressed are obtained as described in Examples 27-29 and cloned into a suitable expression vector. If desired, the nucleic acids may contain the sequences encoding the signal

peptide to facilitate secretion of the expressed protein. For example, the nucleic acid may comprise the sequence of one of SEQ ID NOs: 40-140 and 242-377 listed in Table IV and in the accompanying sequence listing. Alternatively, the nucleic acid may comprise those nucleotides which make up the full coding sequence of one of the sequences of SEO ID NOs: 40-140 and 242-377 as defined in Table IV above.

5

It will be appreciated that should the extent of the full coding sequence (i.e. the sequence encoding the signal peptide and the mature protein resulting from cleavage of the signal peptide) differ from that listed in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the extent of the full coding sequences in the sequences of SEQ ID NOs. 40-140 and 242-377. 10 For example, the sequence of SEQ ID NO: 115 represents an alternatively spliced transcript of a previously identified mRNA.. Accordingly, the scope of any claims herein relating to nucleic acids containing the full coding sequence of one of SEQ ID NOs. 40-140 and 242-377 is not to be construed as excluding any readily identifiable variations from or equivalents to the full coding sequences listed in Table IV Similarly, should the extent of the full length polypeptides differ from those indicated in Table V as a result of any of the preceding factors, the scope of claims relating to polypeptides 15 comprising the amino acid sequence of the full length polypeptides is not to be construed as excluding any readily identifiable variations from or equivalents to the sequences listed in Table V.

Alternatively, the nucleic acid used to express the protein or portion thereof may comprise those nucleotides which encode the mature protein (i.e. the protein created by cleaving the signal peptide off) encoded by one of the sequences of SEQ ID NOs: 40-140 and 242-377 as defined in Table IV above.

20 It will be appreciated that should the extent of the sequence encoding the mature protein differ from that listed in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, posttranslational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the extent of the sequence encoding the mature protein in the sequences of SEQ ID NOs. 40-140 and 242-377. Accordingly, the scope of any claims herein relating to nucleic acids 25 containing the sequence encoding the mature protein encoded by one of SEO ID Nos. 40-140 and 242-377 is not to be construed as excluding any readily identifiable variations from or equivalents to the sequences listed in Table IV. Thus, claims relating to nucleic acids containing the sequence encoding the mature protein encompass equivalents to the sequences listed in Table IV, such as sequences encoding biologically active proteins resulting from post-translational modification, enzymatic cleavage, or other readily identifiable variations from or equivalents to the secreted proteins in 30 addition to cleavage of the signal peptide. Similarly, should the extent of the mature polypeptides differ from those indicated in Table V as a result of any of the preceding factors, the scope of claims relating to polypeptides comprising the sequence of a mature protein included in the sequence of one of SEQ ID NOs. 141-241 and 378-513 is not to be construed as excluding any readily identifiable variations from or equivalents to the sequences listed in Table V. Thus. claims relating to polypeptides comprising the sequence of the mature protein encompass equivalents to the sequences

listed in Table IV, such as biologically active proteins resulting from post-translational modification, enzymatic cleavage, or other readily identifiable variations from or equivalents to the secreted proteins in addition to cleavage of the signal peptide. It will also be appreciated that should the biologically active form of the polypeptides included in the sequence of one of SEQ ID NOs. 141-241 and 378-513 or the nucleic acids encoding the biologically active form of the polypeptides differ from those identified as the mature polypeptide in Table V or the nucleotides encoding the mature polypeptide in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the amino acids in the biologically active form of the polypeptides and the nucleic acids encoding the biologically active form of the polypeptides. In such instances, the claims relating to polypetides comprising the mature protein included in one of SEQ ID NOs. 141-241 and 378-513 or nucleic acids comprising the nucleotides of one of SEQ ID NOs. 40-140 and 242-377 encoding the mature protein shall not be construed to exclude any readily identifiable variations from the sequences listed in Table IV and Table V.

In some embodiments, the nucleic acid used to express the protein or portion thereof may comprise those nucleotides which encode the signal peptide encoded by one of the sequences of SEQ ID NOs: 40-140 and 242-377 as defined in Table IV above.

It will be appreciated that should the extent of the sequence encoding the signal peptide differ from that listed in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the extent of the sequence encoding the signal peptide in the sequences of SEQ ID NOs. 40-140 and 242-377. Accordingly, the scope of any claims herein relating to nucleic acids containing the sequence encoding the signal peptide encoded by one of SEQ ID Nos. 40-140 and 242-377 is not to be construed as excluding any readily identifiable variations from the sequences listed in Table IV. Similarly, should the extent of the signal peptides differ from those indicated in Table V as a result of any of the preceding factors, the scope of claims relating to polypeptides comprising the sequence of a signal peptide included in the sequence of one of SEQ ID Nos. 141-241 and 378-513 is not to be construed as excluding any readily identifiable variations from the sequences listed in Table V.

Alternatively, the nucleic acid may encode a polypeptide comprising at least 10 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In some embodiments, the nucleic acid may encode a polypeptide comprising at least 15 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In other embodiments, the nucleic acid may encode a polypeptide comprising at least 25 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In other embodiments, the nucleic acid may encode a polypeptide comprising at least 60, at least 75, at least 100 or more than 100 consecutive amino acids of one of the sequences of SEQ ID Nos: 141-241 and 378-513.

WO 99/31236 PCT/IB98/02122

The nucleic acids inserted into the expression vectors may also contain sequences upstream of the sequences encoding the signal peptide, such as sequences which regulate expression levels or sequences which confer tissue specific expression.

The nucleic acid encoding the protein or polypeptide to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector may be any of the mammalian, yeast, insect or bacterial expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon context and codon pairing of the sequence may be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, et al., U.S. Patent No. 5,082,767.

The following is provided as one exemplary method to express the proteins encoded by the extended cDNAs corresponding to the 5' ESTs or the nucleic acids described above. First, the methionine initiation codon for the gene and the poly A signal of the gene are identified. If the nucleic acid encoding the polypeptide to be expressed lacks a methionine to serve as the initiation site, an initiating methionine can be introduced next to the first codon of the nucleic acid using conventional techniques. Similarly, if the extended cDNA lacks a poly A signal, this sequence can be added to the construct by, for example, splicing out the Poly A signal from pSG5 (Stratagene) using Bgll and Sall restriction endonuclease enzymes and incorporating it into the mammalian expression vector pXT1 (Stratagene). pXT1 contains the LTRs and a portion of the gag gene from Moloney Murine Leukemia Virus. The position of the LTRs in the construct allow efficient stable transfection. The vector includes the Herpes Simplex Thymidine Kinase promoter and the selectable neomycin gene. The extended cDNA or portion thereof encoding the polypeptide to be expressed is obtained by PCR from the bacterial vector using oligonucleotide primers complementary to the extended cDNA or portion thereof and containing restriction endonuclease sequences for Pst I incorporated into the 5'primer and Bglll at the 5' end of the corresponding cDNA 3' primer, taking care to ensure that the extended cDNA is positioned in frame with the poly A signal. The purified fragment obtained from the resulting PCR reaction is digested with Pstl, blunt ended with an exonuclease, digested with Bgl II, purified and ligated to pXT1, now containing a poly A signal and digested with Bgl II.

The ligated product is transfected into mouse NIH 3T3 cells using Lipofectin (Life Technologies, Inc., Grand Island, New York) under conditions outlined in the product specification. Positive transfectants are selected after growing the transfected cells in 600ug/ml G418 (Sigma, St. Louis, Missouri). Preferably the expressed protein is released into the culture medium, thereby facilitating purification.

Alternatively, the extended cDNAs may be cloned into pED6dpc2 as described above. The resulting pED6dpc2 constructs may be transfected into a suitable host cell, such as COS 1 cells. Methotrexate resistant cells are selected and expanded. Preferably, the protein expressed from the extended cDNA is released into the culture medium thereby facilitating purification.

WO 99/31236 PCT/IB98/02122

.50

Proteins in the culture medium are separated by gel electrophoresis. If desired, the proteins may be ammonium suffate precipitated or separated based on size or charge prior to electrophoresis.

As a control, the expression vector lacking a cDNA insert is introduced into host cells or organisms and the proteins in the medium are harvested. The secreted proteins present in the medium are detected using techniques such as Coomassie or silver staining or using antibodies against the protein encoded by the extended cDNA. Coomassie and silver staining techniques are familiar to those skilled in the art.

Antibodies capable of specifically recognizing the protein of interest may be generated using synthetic 15-mer peptides having a sequence encoded by the appropriate 5' EST, extended cDNA, or portion thereof. The synthetic peptides are injected into mice to generate antibody to the polypeptide encoded by the 5' EST, extended cDNA, or portion thereof.

Secreted proteins from the host cells or organisms containing an expression vector which contains the extended cDNA derived from a 5' EST or a portion thereof are compared to those from the control cells or organism. The presence of a band in the medium from the cells containing the expression vector which is absent in the medium from the control cells indicates that the extended cDNA encodes a secreted protein. Generally, the band corresponding to the protein encoded by the extended cDNA will have a mobility near that expected based on the number of amino acids in the open reading frame of the extended cDNA. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

Alternatively, if the protein expressed from the above expression vectors does not contain sequences directing its secretion, the proteins expressed from host cells containing an expression vector containing an insert encoding a secreted protein or portion thereof can be compared to the proteins expressed in host cells containing the expression vector without an insert. The presence of a band in samples from cells containing the expression vector with an insert which is absent in samples from cells containing the expression vector without an insert indicates that the desired protein or portion thereof is being expressed. Generally, the band will have the mobility expected for the secreted protein or portion thereof. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

The protein encoded by the extended cDNA may be purified using standard immunochromatography techniques.

In such procedures, a solution containing the secreted protein, such as the culture medium or a cell extract, is applied to a column having antibodies against the secreted protein attached to the chromatography matrix. The secreted protein is allowed to bind the immunochromatography column. Thereafter, the column is washed to remove non-specifically bound proteins. The specifically bound secreted protein is then released from the column and recovered using standard techniques.

If antibody production is not possible, the extended cDNA sequence or portion thereof may be incorporated into expression vectors designed for use in purification schemes employing chimeric polypeptides. In such strategies the coding sequence of the extended cDNA or portion thereof is inserted in frame with the gene encoding the other half of

WO 99/31236

20

the chimera. The other half of the chimera may be β-globin or a nickel binding polypeptide encoding sequence. A chromatography matrix having antibody to β-globin or nickel attached thereto is then used to purify the chimeric protein. Protease cleavage sites may be engineered between the β-globin gene or the nickel binding polypeptide and the extended cDNA or portion thereof. Thus, the two polypeptides of the chimera may be separated from one another by protease digestion.

One useful expression vector for generating β-globin chimerics is pSG5 (Stratagene), which encodes rabbit β-globin. Intron II of the rabbit β-globin gene facilitates splicing of the expressed transcript, and the polyadenylation signal incorporated into the construct increases the level of expression. These techniques as described are well known to those skilled in the art of molecular biology. Standard methods are published in methods texts such as Davis et al.,

(Basic Methods in Molecular Biology, L.G. Davis, M.D. Dibner, and J.F. Battey, ed., Elsevier Press, NY, 1986) and many of the methods are available from Stratagene, Life Technologies, Inc., or Promega. Polypeptide may additionally be produced from the construct using in vitro translation systems such as the in vitro ExpressTM Translation Kit (Stratagene).

Following expression and purification of the secreted proteins encoded by the 5' ESTs, extended cDNAs, or fragments thereof, the purified proteins may be tested for the ability to bind to the surface of various cell types as described in Example 31 below. It will be appreciated that a plurality of proteins expressed from these cDNAs may be included in a panel of proteins to be simultaneously evaluated for the activities specifically described below, as well as other biological roles for which assays for determining activity are available.

EXAMPLE 31

Analysis of Secreted Proteins to Determine Whether they Bind to the Cell Surface

The proteins encoded by the 5' ESTs, extended cDNAs, or fragments thereof are cloned into expression vectors such as those described in Example 30. The proteins are purified by size, charge, immunochromatography or other techniques familiar to those skilled in the art. Following purification, the proteins are labeled using techniques known to those skilled in the art. The labeled proteins are incubated with cells or cell lines derived from a variety of organs or tissues to allow the proteins to bind to any receptor present on the cell surface. Following the incubation, the cells are washed to remove non-specifically bound protein. The labeled proteins are detected by autoradiography. Alternatively, unlabeled proteins may be incubated with the cells and detected with antibodies having a detectable label, such as a fluorescent molecule, attached thereto.

Specificity of cell surface binding may be analyzed by conducting a competition analysis in which various amounts of unlabeled protein are incubated along with the labeled protein. The amount of labeled protein bound to the cell surface decreases as the amount of competitive unlabeled protein increases. As a control, various amounts of an unlabeled protein unrelated to the labeled protein is included in some binding reactions. The amount of labeled protein bound to the cell surface does not decrease in binding reactions containing increasing amounts of unrelated unlabeled protein, indicating that the protein encoded by the cDNA binds specifically to the cell surface.

As discussed above, secreted proteins have been shown to have a number of important physiological effects and, consequently, represent a valuable therapeutic resource. The secreted proteins encoded by the extended cDNAs or portions thereof made according to Examples 27-29 may be evaluated to determine their physiological activities as described below.

5 EXAMPLE 32

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Cytokine, Cell Proliferation or Cell Differentiation Activity

As discussed above, secreted proteins may act as cytokines or may affect cellular proliferation or differentiation. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 320, DA2, DA1G, T10, B5, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7c and CMK. The proteins encoded by the above extended cDNAs or portions thereof may be evaluated for their ability to regulate T cell or thymocyte proliferation in assays such as those described above or in the following references: Current Protocols in Immunology, Ed. by J.E. Coligan et al., Greene Publishing Associates and Wiley-Interscience; Takai et al. J. Immunol. 137:3494-3500, 1986. Bertagnolli et al. J. Immunol. 145:1706-1712, 1990. Bertagnolli et al., Cellular Immunology 133:327-341, 1991. Bertagnolli, et al. J. Immunol. 149:3778:3783, 1992; Bowman et al., J. Immunol. 152:1756-1761, 1994.

In addition, numerous assays for cytokine production and/or the proliferation of spleen cells, lymph node cells
and thymocytes are known. These include the techniques disclosed in Current Protocols in Immunology. J.E. Coligan
et al. Eds., Vol 1 pp. 3.12.1-3.12.14 John Wiley and Sons, Toronto. 1994; and Schreiber, R.D. Current Protocols in
Immunology., supra Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

The proteins encoded by the cDNAs may also be assayed for the ability to regulate the proliferation and differentiation of hematopoietic or lymphopoietic cells. Many assays for such activity are familiar to those skilled in the art, including the assays in the following references: Bottomly, K., Davis, L.S. and Lipsky, P.E., Measurement of Human and Murine Interleukin 2 and Interleukin 4, Current Protocols in Immunology., J.E. Coligan et al. Eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 36:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Nordan, R., Measurement of Mouse and Human Interleukin 6 Current Protocols in Immunology, J.E. Coligan et al. Eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Bennett, F., Giannotti, J., Clark, S.C. and Turner, K.J., Measurement of Human Interleukin 11 Current Protocols in Immunology. J.E. Coligan et al. Eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Crarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J., Measurement of Mouse and Human Interleukin 9 Current Protocols in Immunology. J.E. Coligan et al., Eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

The proteins encoded by the cDNAs may also be assayed for their ability to regulate T-cell responses to antigens. Many assays for such activity are familiar to those skilled in the art, including the assays described in the following references: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function), Chapter 6 (Cytokines and Their Cellular Receptors) and Chapter 7, (Immunologic Studies in Humans) in Current Protocols in Immunology, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience; Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Those proteins which exhibit cytokine, cell proliferation, or cell differentiation activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which induction of cell proliferation or differentiation is beneficial. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 33

Assaying the Proteins Expressed from Extended cDNAs or Portions

15

Thereof for Activity as Immune System Regulators

The proteins encoded by the cDNAs may also be evaluated for their effects as immune regulators. For example, the proteins may be evaluated for their activity to influence thymocyte or splenocyte cytotoxicity. Numerous assays for such activity are familiar to those skilled in the art including the assays described in the following references: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function 3.1-3.19) and Chapter 7 (Immunologic studies in Humans) in Current Protocols in Immunology, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

The proteins encoded by the cDNAs may also be evaluated for their effects on T-cell dependent immunoglobulin responses and isotype switching. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Maliszewski, J. Immunol. 144:3028-3033, 1990; Mond, J.J. and Brunswick, M Assays for B Cell Function: *In vitro* Antibody Production, Vol 1 pp. 3.8.1-3.8.16 in Current Protocols in Immunology. J.E. Coligan et al Eds., John Wiley and Sons, Toronto. 1994.

The proteins encoded by the cDNAs may also be evaluated for their effect on immune effector cells, including their effect on Th1 cells and cytotoxic lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Chapter 3 (In Vitro Assays for Mouse Lymphocyte

Function 3.1-3.19) and Chapter 7 (Immunologic Studies in Humans) in Current Protocols in Immunology, J.E. Coligan et al. Eds., Greene Publishing Associates and Wiley-Interscience; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

The proteins encoded by the cDNAs may also be evaluated for their effect on dendritic cell mediated activation of naive T-cells. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

The proteins ercoded by the cDNAs may also be evaluated for their influence on the lifetime of lymphocytes.

Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Those proteins which exhibit activity as immune system regulators activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of immune activity is beneficial. For example, the protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis,

WO 99/31236 PCT/1B98/02122

.55.

myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

5

tolerizing agent.

Using the proteins of the invention it may also be possible to regulate immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T-cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. 10 Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte 15 antigen functions (such as, for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 20 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an 25 immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed 30 using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet call grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4lg fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models

WO 99/31236 PCT/IB98/02122

-56-

of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which 5 promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead 10 to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/pr/pr mice or NZB hybrid mice, murine autoimmuno collagen arthritis, diabetes mellitus in OD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory 20 form of B lymphocyte antigens systemically.

15

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to T cells 25 in vivo, thereby activating the T cells.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be 30 transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having 87-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

A Later Co.

in the state of th

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acids encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and β2 macroglobulin protein or an MHC class II α chain protein and an MHC class II β chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class II or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7·1, B7·2, B7·3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain,can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 34

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Hematopoiesis Regulating Activity

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their hematopoiesis regulating activity. For example, the effect of the proteins on embryonic stem cell differentiation may be evaluated. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their influence on the lifetime of stem cells and stem cell differentiation. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Freshney, M.G. Methylcellulose Colony Forming Assays, in Culture of Hernatopoietic Cells. R.I. Freshney, et al. Eds. pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; McNiece, I.K. and Briddell, R.A. Primitive Hernatopoietic Colony Forming Cells with High Proliferative Potential, in Culture of Hernatopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hernatology 22:353-359, 1994; Ploemacher, R.E. Cobblestone Area Forming Cell Assay, In Culture of Hernatopoietic Cells. R.I. Freshney, et al. Eds. pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Spooncer, E., Dexter, M. and Allen, T. Long Term

Bone Marrow Cultures in the Presence of Stromal Cells, in Culture of Hematopoietic Cells. R.I. Freshney, et al. Eds.

pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; and Sutherland, H.J. Long Term Culture Initiating Cell Assay, in Culture of Hematopoietic Cells. R.I. Freshney, et al. Eds. pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Those proteins which exhibit hematopoiesis regulatory activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of hematopoeisis is beneficial. For example, a protein of the present 5 invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid 10 cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelosuppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem 15 cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantion, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or 20 genetically manipulated for gene therapy. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 35

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Tissue Growth

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effect on tissue growth. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in International Patent Publication No. W095/16035, International Patent Publication No. W095/05846 and International Patent Publication No. W091/07491.

Assays for wound healing activity include, without limitation, those described in: Winter, <u>Epidermal Wound</u>

30 <u>Healing</u>, pps. 71-112 (Maibach, H1 and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Those proteins which are involved in the regulation of tissue growth may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of tissue growth is beneficial. For example, a protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or

WO 99/31236 PCT/IB98/02122

nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and 5 other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair 10 processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming calls or induce differentiation of progenitors of bone-forming calls. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

15

30

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to 20 tenden or ligament tissue, as well as use in the improved fixation of tenden or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate 25 growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e., for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Orager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium) muscle

(smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to generate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

20

15

5

EXAMPLE 36

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Reproductive Hormones or Cell Movement

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their ability to regulate reproductive hormones, such as follicle stimulating hormone. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986. Chapter 6.12 (Measurement of Alpha and Beta Chemokines) Current Protocols in Immunology, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Intersciece; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al. Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.

Those proteins which exhibit activity as reproductive hormones or regulators of cell movement may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of reproductive hormones or cell movement are beneficial. For example, a protein of the present invention may also exhibit activin- or inhibin-related

activities. Inhibins are characterized by their ability to inhibit the release of folicies stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of folic stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin α family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals.

Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin-B group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 36A

15

25

30

Assaying the Proteins Expressed from Extended cDNAs or

And Additional Portions Thereof for Chemotactic/Chemokinetic Activity

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for chemotactic/chemokinetic activity. For example, a protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, cosinophils, epithelial and/or endothelial cells. Chemotactic and chmokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhension of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, O.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12,

Measurement of alpha and beta Chemokincs 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Mueller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol, 153:1762-1768, 1994.

EXAMPLE 37

5

Assaying the Proteins Expressed from Extended cDNAs or

Portions Thereof for Regulation of Blood Clotting

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effects on blood clotting. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res.

45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

Those proteins which are involved in the regulation of blood clotting may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of blood clotting is beneficial. For example, a protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulations disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke). Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 38

Assaving the Proteins Expressed from Extended cDNAs or Portions Thereof for Involvement in Receptor/Ligand Interactions

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for their involvement in receptor/ligand interactions. Numerous assays for such involvement are familiar to those skilled in the art, including the assays disclosed in the following references: Chapter 7.28 (Measurement of Cellular Adhesion under Static Conditions 7.28.1-7.28.22) in Current Protocols in Immunology, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience; Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160, 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995; Gyuris et al., Cell 75:791-803, 1993.

For example, the proteins of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion

-63-

molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune respones). Receptors and ligands are also useful for screening of potential paptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as 5 inhibitors of receptor/ligand interactions.

EXAMPLE 38A

Assaving the Proteins Expressed from Extended cDNAs or Portions

Thereof for Anti-Inflammatory Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for ami-inflammatory 10 activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including 15 without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusioninury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease. Crohn's disease or resulting from over production of cytokines such as INF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

20

30

EXAMPLE 38B

Assaying the Proteins Expressed from Extended cDNAs or

Portions Thereof for Tumor Inhibition Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for tumor inhibition activity. In addition to the activities described above for immunological treatment or prevention of tumors, a protein of 25 the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, climinating or inhibiting factors, agents or cell types which promote tumor growth.

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or

circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or climination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

EXAMPLE 39

Identification of Proteins which Interact with

Polypeptides Encoded by Extended cDNAs

Proteins which interact with the polypeptides encoded by extended cDNAs or portions thereof, such as

receptor proteins, may be identified using two hybrid systems such as the Matchmaker Two Hybrid System 2 (Catalog No. K1604-1, Clontech). As described in the manual accompanying the Matchmaker Two Hybrid System 2 (Catalog No. K1604-1, Clontech), the extended cDNAs or portions thereof, are inserted into an expression vector such that they are in frame with DNA encoding the DNA binding domain of the yeast transcriptional activator GAL4. cDNAs in a cDNA library which encode proteins which might interact with the polypeptides encoded by the extended cDNAs or portions thereof are inserted into a second expression vector such that they are in frame with DNA encoding the activation domain of GAL4. The two expression plasmids are transformed into yeast and the yeast are plated on selection medium which selects for expression of selectable markers on each of the expression vectors as well as GAL4 dependent expression of the HIS3 gene. Transformants capable of growing on medium lacking histidine are screened for GAL4 dependent lacZ expression. Those cells which are positive in both the histidine selection and the lacZ assay contain plasmids encoding proteins which interact with the polypeptide encoded by the extended cDNAs or portions thereof.

Alternatively, the system described in Lustig et al., Methods in Enzymology 283: 83-99 (1997) may be used for identifying molecules which interact with the polypeptides encoded by extended cDNAs. In such systems, in vitro transcription reactions are performed on a pool of vectors containing extended cDNA inserts cloned downstream of a promoter which drives in vitro transcription. The resulting pools of mRNAs are introduced into Xenopus laevis occytes.

30 The oocytes are then assayed for a desired acitivity.

Alternatively, the pooled *in vitro* transcription products produced as described above may be translated *in vitro*.

The pooled *in vitro* translation products can be assayed for a desired activity or for interaction with a known polypeptide.

Proteins or other molecules interacting with polypeptides encoded by extended cDNAs can be found by a variety of additional techniques. In one method, affinity columns containing the polypeptide encoded by the extended cDNA or a portion thereof can be constructed. In some versions, of this method the affinity column contains chimeric proteins in which the protein encoded by the extended cDNA or a portion thereof is fused to glutathione S-transferase.

5 A mixture of cellular proteins or pool of expressed proteins as described above and is applied to the affinity column. Proteins interacting with the polypeptide attached to the column can then be isolated and analyzed on 2-D electrophoresis gel as described in Ramunson et al. Electrophoresis, 18, 588-598 (1997). Alternatively, the proteins retained on the affinity column can be purified by electrophoresis based methods and sequenced. The same method can be used to isolate antibodies, to screen phage display products, or to screen phage display human antibodies.

Proteins interacting with polypeptides encoded by extended cDNAs or portions thereof can also be screened by using an Optical Biosensor as described in Edwards & Leatherbarrow, Analytical Biochemistry, 246, 1-6 (1997). The main advantage of the method is that it allows the determination of the association rate between the protein and other interacting molecules. Thus, it is possible to specifically select interacting molecules with a high or low association rate. Typically a target molecule is linked to the sensor surface (through a carboxymeth) dextran matrix) and a sample of test 15 molecules is placed in contact with the target molecules. The binding of a test molecule to the target molecule causes a change in the refractive index and/ or thickness. This change is detected by the Biosensor provided it occurs in the evanescent field (which extend a few hundred manometers from the sensor surface). In these screening assays, the target molecule can be one of the polypeptides encoded by extended cDNAs or a portion thereof and the test sample can be a collection of proteins extracted from tissues or cells, a pool of expressed proteins, combinatorial peptide and/ or 20 chemical libraries, or phage displayed peptides. The tissues or cells from which the test proteins are extracted can originate from any species.

In other methods, a target protein is immobilized and the test population is a collection of unique polypeptides encoded by the extended cDNAs or portions thereof.

To study the interaction of the proteins encoded by the extended cDNAs or portions thereof with drugs, the 25 microdialysis coupled to HPLC method described by Wang et al., Chromatographia, 44, 205-208(1997) or the affinity capillary electrophoresis method described by Busch et al., J. Chromatogr. 777:311-328 (1997), the disclosures of which are incorporated herein by referenc can be used.

The system described in U.S. Patent No. 5,654,150 may also be used to identify molecules which interact with the polypeptides encoded by the extended cDNAs. In this system, pools of extended cDNAs are transcribed and 30 translated in vitro and the reaction products are assayed for interaction with a known polypeptide or antibody.

It will be appreciated by those skilled in the art that the proteins expressed from the extended cDNAs or portions may be assayed for numerous activities in addition to those specifically enumerated above. For example, the expressed proteins may be evaluated for applications involving control and regulation of inflammation, tumor

proliferation or metastasis, infection, or other clinical conditions. In addition, the proteins expressed from the extended cDNAs or portions thereof may be useful as nutritional agents or cosmetic agents.

The proteins expressed from the extended cDNAs or portions thereof may be used to generate antibodies capable of specifically binding to the expressed protein or fragments thereof as described in Example 40 below. The antibodies may capable of binding a full length protein encoded by one of the sequences of SEQ ID NOs. 40-140 and 242-377, a mature protein encoded by one of the sequences of SEQ ID NOs. 40-140 and 242-377. Alternatively, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 10 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In some embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 15 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In other embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 25 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In further embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 25 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In further embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 40 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513.

EXAMPLE 40

Production of an Antibody to a Human Protein

Substantially pure protein or polypeptide is isolated from the transfected or transformed cells as described in Example 30. The concentration of protein in the final preparation is adjusted, for example, by concentration on an Amicon filter device, to the level of a few micrograms/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows:

A. Monoclonal Antibody Production by Hybridoma Fusion

Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, G. and Milstein, C., Nature 256:495 (1975) or derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as Elisa, as originally described by Engvall, E., Meth. Enzymol. 70:419 (1980), and derivative methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. et al. Basic Methods in Molecular Biology Elsevier, New York. Section 21-2.

В. Polycional Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogenous epitopes of a single protein can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom described above, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors 5 related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than others and may require the use of carriers and adjuvant. Also, host animals vary in response to site of inoculations and dose, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis, J. et al. J. Clin. Endocrinol. Metab. 33:988-991 (1971).

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. et al., Chap. 19 in: Handbook of Experimental Immunology D. Wier (ed) Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12 μ M). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as 15 described, for example, by Fisher, D., Chap. 42 in: Manual of Clinical Immunology, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D.C. (1980).

Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic 20 compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

V. Use of Extended cDNAs or Portions Thereof as Reagents

The extended cDNAs of the present invention may be used as reagents in isolation procedures, diagnostic assays, and forensic procedures. For example, sequences from the extended cDNAs (or genomic DNAs obtainable 25 therefrom) may be detectably labeled and used as probes to isolate other sequences capable of hybridizing to them. In addition, sequences from the extended cDNAs (or genomic DNAs obtainable therefrom) may be used to design PCR primers to be used in isolation, diagnostic, or forensic procedures.

EXAMPLE 41

Preparation of PCR Primers and Amplification of DNA

30 The extended cDNAs (or genomic DNAs obtainable therefrom) may be used to prepare PCR primers for a variety of applications, including isolation procedures for cloning nucleic acids capable of hybridizing to such sequences, diagnostic techniques and forensic techniques. The PCR primers are at least 10 bases, and preferably at least 12, 15, or 17 bases in length. More preferably, the PCR primers are at least 20:30 bases in length. In some embodiments, the PCR primers may be more than 30 bases in length. It is preferred that the primer pairs have approximately the same G/C

ratio, so that melting temperatures are approximately the same. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see Molecular Cloning to Genetic Engineering White, B.A. Ed. in Methods in Molecular Biology 67: Humana Press, Totowa 1997. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid sample along with dNTPs and a thermostable polymerase such as Taq polymerase, Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation, hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites.

10

EXAMPLE 42

Use of Extended cDNAs as Probes

Probes derived from extended cDNAs or portions thereof (or genomic DNAs obtainable therefrom) may be labeled with detectable labels familiar to those skilled in the art, including radioisotopes and non-radioactive labels, to provide a detectable probe. The detectable probe may be single stranded or double stranded and may be made using techniques known in the art, including in vitro transcription, nick translation, or kinase reactions. A nucleic acid sample containing a sequence capable of hybridizing to the labeled probe is contacted with the labeled probe. If the nucleic acid in the sample is double stranded, it may be denatured prior to contacting the probe. In some applications, the nucleic acid sample may be immobilized on a surface such as a nitrocellulose or nylon membrane. The nucleic acid sample may comprise nucleic acids obtained from a variety of sources, including genomic DNA, cDNA/tibraries, RNA, or tissue samples.

Procedures used to detect the presence of nucleic acids capable of hybridizing to the detectable probe include well known techniques such as Southern blotting, Northern blotting, dot blotting, colony hybridization, and plaque hybridization. In some applications, the nucleic acid capable of hybridizing to the labeled probe may be cloned into vectors such as expression vectors, sequencing vectors, or in vitro transcription vectors to facilitate the characterization and expression of the hybridizing nucleic acids in the sample. For example, such techniques may be used to isolate and clone sequences in a genomic library or cDNA library which are capable of hybridizing to the detectable probe as described in Example 30 above.

PCR primers made as described in Example 41 above may be used in forensic analyses, such as the DNA fingerprinting techniques described in Examples 43-47 below. Such analyses may utilize detectable probes or primers based on the sequences of the extended cDNAs isolated using the 5' ESTs (or genomic DNAs obtainable therefrom).

EXAMPLE 43

Forensic Matching by DNA Sequencing

In one exemplary method, DNA samples are isolated from forensic specimens of, for example, hair, semen, blood or skin cells by conventional methods. A panel of PCR primers based on a number of the extended cDNAs (or

genomic DNAs obtainable therefrom), is then utilized in accordance with Example 41 to amplify DNA of approximately 100-200 bases in length from the forensic specimen. Corresponding sequences are obtained from a test subject. Each of these identification DNAs is then sequenced using standard techniques, and a simple database comparison determines the differences, if any, between the sequences from the subject and those from the sample. Statistically significant differences between the suspect's DNA sequences and those from the sample conclusively prove a lack of identity. This lack of identity can be proven, for example, with only one sequence. Identity, on the other hand, should be demonstrated with a large number of sequences, all matching. Preferably, a minimum of 50 statistically identical sequences of 100 bases in length are used to prove identity between the suspect and the sample.

EXAMPLE 44

10

Positive Identification by DNA Sequencing

The technique outlined in the previous example may also be used on a larger scale to provide a unique fingerprint-type identification of any individual. In this technique, primers are prepared from a large number of sequences from Table IV and the appended sequence listing. Preferably, 20 to 50 different primers are used. These primers are used to obtain a corresponding number of PCR-generated DNA segments from the individual in question in accordance with Example 41. Each of these DNA segments is sequenced, using the methods set forth in Example 43. The database of sequences generated through this procedure uniquely identifies the individual from whom the sequences were obtained. The same panel of primers may then be used at any later time to absolutely correlate tissue or other biological specimen with that individual.

EXAMPLE 45

20

Southern Blot Forensic Identification

The procedure of Example 44 is repeated to obtain a panel of at least 10 amplified sequences from an individual and a specimen. Preferably, the panel contains at least 50 amplified sequences. More preferably, the panel contains 100 amplified sequences. In some embodiments, the panel contains 200 amplified sequences. This PCR-generated DNA is then digested with one or a combination of, preferably, four base specific restriction enzymes. Such enzymes are commercially available and known to those of skill in the art. After digestion, the resultant gene fragments are size separated in multiple duplicate wells on an agarose gel and transferred to nitrocellulose using Southern biotting techniques well known to those with skill in the art. For a review of Southern blotting see Davis et al. (Basic Methods in Molecular Biology, 1986, Elsevier Press. pp 62-65).

A panel of probes based on the sequences of the extended cDNAs (or genomic DNAs obtainable therefrom), or fragments thereof of at least 10 bases, are radioactively or colorimetrically labeled using methods known in the art, such as nick translation or end labeling, and hybridized to the Southern blot using techniques known in the art (Davis et al., supra). Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30

nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In other embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom).

Preferably, at least 5 to 10 of these labeled probes are used, and more preferably at least about 20 or 30 are 5 used to provide a unique pattern. The resultant bands appearing from the hybridization of a large sample of extended cDNAs (or genomic DNAs obtainable therefrom) will be a unique identifier. Since the restriction enzyme cleavage will be different for every individual, the band pattern on the Southern blot will also be unique. Increasing the number of extended cDNA probes will provide a statistically higher level of confidence in the identification since there will be an increased number of sets of bands used for identification.

10

25

EXAMPLE 46

Dot Blot Identification Procedure

Another technique for identifying individuals using the extended cDNA sequences disclosed herein utilizes a dot blot hybridization technique.

Genomic DNA is isolated from nuclei of subject to be identified. Oligonucleotide probes of approximately 30 bp 15 in length are synthesized that correspond to at least 10, preferably 50 sequences from the extended cDNAs or genomic DNAs obtainable therefrom. The probes are used to hybridize to the genomic DNA through conditions known to those in the art. The oligonucleotides are end labeled with P³² using polynucleotide kinase (Pharmacia). Dot Blots are created by spotting the genomic DNA onto nitrocellulose or the like using a vacuum dot blot manifold (BioRad, Richmond California). The nitrocellulose filter containing the genomic sequences is baked or UV linked to the filter, prehybridized and 20 hybridized with labeled probe using techniques known in the art (Davis et al. supra). The 32P labeled DNA fragments are sequentially hybridized with successively stringent conditions to detect minimal differences between the 30 bp sequence and the DNA. Tetramethylammonium chloride is useful for identifying clones containing small numbers of nucleotide mismatches (Wood et al., Proc. Natl. Acad. Sci. USA 82(6):1585-1588 (1985)). A unique pattern of dots distinguishes one individual from another individual.

Extended cDNAs or oligonucleotides containing at least 10 consecutive bases from these sequences can be used as probes in the following alternative fingerprinting technique. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30 nucleotides from the extended cDNA (or genomic 30 DNAs obtainable therefrom). In other embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom).

Preferably, a plurality of probes having sequences from different genes are used in the alternative fingerprinting technique. Example 47 below provides a representative alternative fingerprinting procedure in which the probes are derived from extended cDNAs.

EXAMPLE 47

5

Alternative "Fingerprint" Identification Technique

20-mer oligonucleotides are prepared from a large number, e.g. 50, 100, or 200, of extended cDNA sequences (or genomic DNAs obtainable therefrom) using commercially available oligonucleotide services such as Genset, Paris, France. Cell samples from the test subject are processed for DNA using techniques well known to those with skill in the art. The nucleic acid is digested with restriction enzymes such as EcoRI and Xbal. Following digestion, samples are applied to wells for electrophoresis. The procedure, as known in the art, may be modified to accommodate polyacrylamide electrophoresis, however in this example, samples containing 5 ug of DNA are loaded into wells and separated on 0.8% agarose gels. The gels are transferred onto nitrocellulose using standard Southern blotting techniques.

10 ng of each of the oligonucleotides are pooled and end-labeled with P³². The nitrocellulose is prehybridized
with blocking solution and hybridized with the labeled probes. Following hybridization and washing, the nitrocellulose
filter is exposed to X-Omat AR X-ray film. The resulting hybridization pattern will be unique for each individual.

It is additionally contemplated within this example that the number of probe sequences used can be varied for additional accuracy or clarity.

The antibodies generated in Examples 30 and 40 above may be used to identify the tissue type or cell species from which a sample is derived as described above.

EXAMPLE 48

Identification of Tissue Types or Cell Species by Means of Labeled Tissue Specific Antibodies

Identification of specific tissues is accomplished by the visualization of tissue specific antigens by means of antibody preparations according to Examples 30 and 40 which are conjugated, directly or indirectly to a detectable marker. Selected labeled antibody species bind to their specific antigen binding partner in tissue sections, cell suspensions, or in extracts of soluble proteins from a tissue sample to provide a pattern for qualitative or semi-qualitative interpretation.

Antisera for these procedures must have a potency exceeding that of the native preparation, and for that
reason, antibodies are concentrated to a mg/ml level by isolation of the gamma globulin fraction, for example, by ionexchange chromatography or by ammonium sulfate fractionation. Also, to provide the most specific antisera, unwanted
antibodies, for example to common proteins, must be removed from the gamma globulin fraction, for example by means
of insoluble immunoabsorbents, before the antibodies are labeled with the marker. Either monoclonal or heterologous
antisera is suitable for either procedure.

20

A. Immunohistochemical Techniques

Purified, high-titer antibodies, prepared as described above, are conjugated to a detectable marker, as described, for example, by Fudenberg, H., Chap. 26 in: **Basic 503 Clinical Immunology**, 3rd Ed. Lange, Los Altos, California (1980) or Rose, N. et al., Chap. 12 in: **Methods in Immunodiagnosis**, 2d Ed. John Wiley 503 Sons, New York (1980).

A fluorescent marker, either fluorescein or rhodamine, is preferred, but antibodies can also be labeled with an enzyme that supports a color producing reaction with a substrate, such as horseradish peroxidase. Markers can be added to tissue-bound antibody in a second step, as described below. Alternatively, the specific antitissue antibodies can be labeled with ferritin or other electron dense particles, and localization of the ferritin coupled antigen-antibody complexes achieved by means of an electron microscope. In yet another approach, the antibodies are radiolabeled, with, for example ¹²⁵I, and detected by overlaying the antibody treated preparation with photographic emulsion.

Preparations to carry out the procedures can comprise monoclonal or polyclonal antibodies to a single protein or peptide identified as specific to a tissue type, for example, brain tissue, or antibody preparations to several antigenically distinct tissue specific antigens can be used in panels, independently or in mixtures, as required.

Tissue sections and cell suspensions are prepared for immunohistochemical examination according to common histological techniques. Multiple cryostat sections (about 4 µm, unfixed) of the unknown tissue and known control, are mounted and each slide covered with different dilutions of the antibody preparation. Sections of known and unknown tissues should also be treated with preparations to provide a positive control, a negative control, for example, pre-immune sera, and a control for non-specific staining, for example, buffer.

Treated sections are incubated in a humid chamber for 30 min at room temperature, rinsed, then washed in buffer for 30-45 min. Excess fluid is blotted away, and the marker developed.

If the tissue specific antibody was not labeled in the first incubation, it can be labeled at this time in a second antibody-antibody reaction, for example, by adding fluorescein- or enzyme-conjugated antibody against the immunoglobulin class of the antiserum-producing species, for example, fluorescein labeled antibody to mouse IgG. Such labeled sera are commercially available.

The antigen found in the tissues by the above procedure can be quantified by measuring the intensity of color or fluorescence on the tissue section, and calibrating that signal using appropriate standards.

B. Identification of Tissue Specific Soluble Proteins

The visualization of tissue specific proteins and identification of unknown tissues from that procedure is

carried out using the labeled antibody reagents and detection strategy as described for immunohistochemistry; however
the sample is prepared according to an electrophoretic technique to distribute the proteins extracted from the tissue in
an orderly array on the basis of molecular weight for detection.

A tissue sample is homogenized using a Virtis apparatus; cell suspensions are disrupted by Dounce homogenization or osmotic lysis, using detergents in either case as required to disrupt cell membranes, as is the practice

in the art. Insoluble cell components such as nuclei, microsomes, and membrane fragments are removed by ultracentrifugation, and the soluble protein-containing fraction concentrated if necessary and reserved for analysis.

A sample of the soluble protein solution is resolved into individual protein species by conventional SDS polyacrylamide electrophoresis as described, for example, by Davis, L. et al., Section 19-2 in: Basic Methods in 5 Molecular Biology (P. Leder, ed), Elsevier, New York (1986), using a range of amounts of polyacrylamide in a set of gels to resolve the entire molecular weight range of proteins to be detected in the sample. A size marker is run in parallel for purposes of estimating molecular weights of the constituent proteins. Sample size for analysis is a convenient volume of from 5 to 55 μ l, and containing from about 1 to 100 μ g protein. An aliquot of each of the resolved proteins is transferred by blotting to a nitrocellulose filter paper, a process that maintains the pattern of resolution. Multiple copies 10 are prepared. The procedure, known as Western Blot Analysis, is well described in Davis, L. et al., (above) Section 19-3. One set of nitrocellulose blots is stained with Coomassie Blue dye to visualize the entire set of proteins for comparison with the antibody bound proteins. The remaining nitrocellulose filters are then incubated with a solution of one or more specific antisera to tissue specific proteins prepared as described in Examples 30 and 40. In this procedure, as in procedure A above, appropriate positive and negative sample and reagent controls are run.

In either procedure A or B, a detectable label can be attached to the primary tissue antigen-primary antibody complex according to various strategies and permutations thereof. In a straightforward approach, the primary specific antibody can be labeled; alternatively, the unlabeled complex can be bound by a labeled secondary anti-lgG antibody. In other approaches, either the primary or secondary antibody is conjugated to a biotin molécule, which can, in a subsequent step, bind an avidin conjugated marker. According to yet another strategy, enzyme labeled or radioactive 20 protein A, which has the property of binding to any IgG, is bound in a final step to either the primary or secondary antibody.

The visualization of tissue specific antigen binding at levels above those seen in control tissues to one or more tissue specific antibodies, prepared from the gene sequences identified from extended cDNA sequences, can identify tissues of unknown origin, for example, forensic samples, or differentiated tumor tissue that has metastasized to foreign 25 bodily sites.

In addition to their applications in forensics and identification, extended cDNAs (or genomic DNAs obtainable therefrom) may be mapped to their chromosomal locations. Example 49 below describes radiation hybrid (RH) mapping of human chromosomal regions using extended cDNAs. Example 50 below describes a representative procedure for mapping an extended cDNA (or a genomic DNA obtainable therefrom) to its location on a human chromosome. Example 30 51 below describes mapping of extended cDNAs (or genomic DNAs obtainable therefrom) on metaphase chromosomes by Fluorescence In Situ Hybridization (FISH).

EXAMPLE 49

Radiation hybrid mapping of Extended cDNAs to the human genome

Radiation hybrid (RH) mapping is a somatic cell genetic approach that can be used for high resolution mapping of the human genome. In this approach, cell lines containing one or more human chromosomes are lethally irradiated, breaking each chromosome into fragments whose size depends on the radiation dose. These fragments are rescued by fusion with cultured rodent cells, yielding subclones containing different portions of the human genome. This technique is described by Benham et al. (*Genomics* 4:509-517, 1989) and Cox et al., (*Science* 250:245-250, 1990). The random and independent nature of the subclones permits efficient mapping of any human genome marker. Human DNA isolated from a panel of 80-100 cell lines provides a mapping reagent for ordering extended cDNAs (or genomic DNAs obtainable therefrom). In this approach, the frequency of breakage between markers is used to measure distance, allowing construction of fine resolution maps as has been done using conventional ESTs (Schuler et al., *Science* 274:540-546, 1996).

RH mapping has been used to generate a high-resolution whole genome radiation hybrid map of human chromosome 17q22-q25.3 across the genes for growth hormone (GH) and thyr idine kinase (TK) (Foster et al., Genomics 33:185-192, 1996), the region surrounding the Gorlin syndrome gene (Obermayr et al., Eur. J. Hum. Genet. 4:242-245, 1996), 60 loci covering the entire short arm of chromosome 12 (Raeymaekers et al., Genomics 29:170-178, 1995), the region of human chromosome 22 containing the neurofibromatosis type 2 locus (Frazer et al., Genomics 14:574-584, 1992) and 13 loci on the long arm of chromosome 5 (Warrington et al., Genomics 11:701-708, 1991).

EXAMPLE 50

Mapping of Extended cDNAs to Human

Chromosomes using PCR techniques

Extended cDNAs (or genomic DNAs obtainable therefrom) may be assigned to human chromosomes using PCR based methodologies. In such approaches, oligonucleotide primer pairs are designed from the extended cDNA sequence (or the sequence of a genomic DNA obtainable therefrom) to minimize the chance of amplifying through an intron. Preferably, the oligonucleotide primers are 18-23 bp in length and are designed for PCR amplification. The creation of PCR primers from known sequences is well known to those with skill in the art. For a review of PCR technology see Erlich, H.A., PCR Technology; Principles and Applications for DNA Amplification. 1992. W.H. Freeman and Co., New York.

The primers are used in polymerase chain reactions (PCR) to amplify templates from total human genomic DNA. PCR conditions are as follows: 60 ng of genomic DNA is used as a template for PCR with 80 ng of each oligonucleotide primer, 0.6 unit of Taq polymerase, and 1 µCu of a ³²P labeled deoxycytidine triphosphate. The PCR is performed in a microplate thermocycler (Techne) under the following conditions: 30 cycles of 94°C, 1.4 min; 55°C, 2 min; and 72°C, 2 min; with a final extension at 72°C for 10 min. The amplified products are analyzed on a 6% polyacrylamide sequencing gel and visualized by autoradiography. If the length of the resulting PCR product is identical to the distance between the ends of the primer sequences in the extended cDNA from which the primers are derived, then the PCR reaction is repeated with DNA templates from two panels of human-rodent somatic cell hybrids. BIOS

PCRable DNA (BIOS Corporation) and NIGMS Human-Rodent Somatic Cell Hybrid Mapping Panel Number 1 (NIGMS, Camden, NJ).

PCR is used to screen a series of somatic cell hybrid cell lines containing defined sets of human chromosomes for the presence of a given extended cDNA (or genomic DNA obtainable therefrom). DNA is isolated from the somatic hybrids and used as starting templates for PCR reactions using the primer pairs from the extended cDNAs (or genomic DNAs obtainable therefrom). Only those somatic cell hybrids with chromosomes containing the human gene corresponding to the extended cDNA (or genomic DNA obtainable therefrom) will yield an amplified fragment. The extended cDNAs (or genomic DNAs obtainable therefrom) are assigned to a chromosome by analysis of the segregation pattern of PCR products from the somatic hybrid DNA templates. The single human chromosome present in all cell hybrids that give rise to an amplified fragment is the chromosome containing that extended cDNA (or genomic DNA obtainable therefrom). For a review of techniques and analysis of results from somatic cell gene mapping experiments. (See Ledbetter et al., Genomics 6:475-481 (1990).)

Alternatively, the extended cDNAs (or genomic DNAs obtainable therefrom) may be mapped to individual chromosomes using FISH as described in Example 51 below.

15

EXAMPLE 51

Mapping of Extended 5' ESTs to Chromosomes

Using Fluorescence in situ Hybridization

Fluorescence in situ hybridization allows the extended cDNA (or genomic DNA obtainable therefrom) to be mapped to a particular location on a given chromosome. The chromosomes to be used for fluorescence in situ hybridization techniques may be obtained from a variety of sources including cell cultures, tissues, or whole blood.

In a preferred embodiment, chromosomal localization of an extended cDNA (or genomic DNA obtainable therefrom) is obtained by FISH as described by Cherif et al. *VProc. Natl. Acad. Sci. U.S.A.*, 87:6639-6643, 1990).

Metaphase chromosomes are prepared from phytohemagglutinin (PHA)-stimulated blood cell donors. PHA-stimulated lymphocytes from healthy males are cultured for 72 h in RPMI-1640 medium. For synchronization, methotrexate (10 µg/ml) is added for 17 h, followed by addition of 5-bromodeoxyuridine (5-BudR, 0.1 mM) for 6 h. Colcemid (1 µg/ml) is added for the last 15 min before harvesting the cells. Cells are collected, washed in RPMI, incubated with a hypotonic solution of KCI (75 mM) at 37°C for 15 min and fixed in three changes of methanol:acetic acid (3:1). The cell suspension is dropped onto a glass slide and air dried. The extended cDNA (or genomic DNA obtainable therefrom) is labeled with biotin-16 dUTP by nick translation according to the manufacturer's instructions (Bethesda Research Laboratories, Bethesda, MD), purified using a Sephadex G-50 column (Pharmacia, Upssala, Sweden) and precipitated. Just prior to hybridization, the DNA pellet is dissolved in hybridization buffer (50% formamide, 2 x SSC, 10% dextran sulfate, 1 mg/ml sonicated salmon sperm DNA, pH 7) and the probe is denatured at 70°C for 5-10 min.

Slides kept at -20°C are treated for 1 h at 37°C with RNase A (100 μ g/ml), rinsed three times in 2 X SSC and dehydrated in an ethanol series. Chromosome preparations are denatured in 70% formamide, 2 X SSC for 2 min at

70°C, then dehydrated at 4°C. The slides are treated with proteinase K (10 μg/100 ml in 20 mM Tris-HCl, 2 mM CaCl₂) at 37°C for 8 min and dehydrated. The hybridization mixture containing the probe is placed on the slide, covered with a coverslip, sealed with rubber cement and incubated overnight in a humid chamber at 37°C. After hybridization and post-hybridization washes, the biotinylated probe is detected by avidin-FITC and amplified with additional layers of biotinylated goat anti-avidin and avidin-FITC. For chromosomal localization, fluorescent R-bands are obtained as previously described (Cherif et al., supra.). The slides are observed under a LEICA fluorescence microscope (DMRXA). Chromosomes are counterstained with propidium iodide and the fluorescent signal of the probe appears as two symmetrical yellow-green spots on both chromatids of the fluorescent R-band chromosome (red). Thus, a particular extended cDNA (or genomic DNA obtainable therefrom) may be localized to a particular cytogenetic R-band on a given chromosome.

Once the extended cDNAs (or genomic DNAs obtainable therefrom) have been assigned to particular chromosomes using the techniques described in Examples 49-51 above, they may be utilized to construct a high resolution map of the chromosomes on which they are located or to identify the chromosomes in a sample.

EXAMPLE 52

15

Use of Extended cDNAs to Construct or Expand Chromosome Maps

Chromosome mapping involves assigning a given unique sequence to a particular chromosome as described above. Once the unique sequence has been mapped to a given chromosome, it is ordered relative to other unique sequences located on the same chromosome. One approach to chromosome mapping utilizes a series of yeast artificial chromosomes (YACs) bearing several thousand long inserts derived from the chromosomes of the organism from which the extended cDNAs (or genomic DNAs obtainable therefrom) are obtained. This approach is described in Ramaiah Nagaraja et al. Genome Research 7:210-222, March 1997. Briefly, in this approach each chromosome is broken into overlapping pieces which are inserted into the YAC vector. The YAC inserts are screened using PCR or other methods to determine whether they include the extended cDNA (or genomic DNA obtainable therefrom) whose position is to be determined. Once an insert has been found which includes the extended cDNA (or genomic DNA obtainable therefrom), the insert can be analyzed by PCR or other methods to determine whether the insert also contains other sequences known to be on the chromosome or in the region from which the extended cDNA (or genomic DNA obtainable therefrom) was derived. This process can be repeated for each insert in the YAC library to determine the location of each of the extended cDNAs (or genomic DNAs obtainable therefrom) relative to one another and to other known chromosomal markers. In this way, a high resolution map of the distribution of numerous unique markers along each of the organisms of the organisms and the obtained.

As described in Example 53 below extended cDNAs (or genomic DNAs obtainable therefrom) may also be used to identify genes associated with a particular phenotype, such as hereditary disease or drug response.

EXAMPLE 53

Identification of genes associated with hereditary diseases or drug response

This example illustrates an approach useful for the association of extended cDNAs (or genomic DNAs obtainable therefrom) with particular phenotypic characteristics. In this example, a particular extended cDNA (or genomic DNA obtainable therefrom) is used as a test probe to associate that extended cDNA (or genomic DNA obtainable therefrom) with a particular phenotypic characteristic.

Extended cDNAs (or genomic DNAs obtainable therefrom) are mapped to a particular location on a human chromosome using techniques such as those described in Examples 49 and 50 or other techniques known in the art. A search of Mendelian Inheritance in Man (V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library) reveals the region of the human chromosome which contains the extended cDNA (or genomic DNA obtainable therefrom) to be a very gene rich region containing several known genes and several 10 diseases or phenotypes for which genes have not been identified. The gene corresponding to this extended cDNA (or genomic DNA obtainable therefrom) thus becomes an immediate candidate for each of these genetic diseases.

Cells from patients with these diseases or phenotypes are isolated and expanded in culture. PCR primers from the extended cDNA (or genomic DNA obtainable therefrom) are used to screen genomic DNA, mRNA or cDNA obtained from the patients. Extended cDNAs (or genomic DNAs obtainable therefrom) that are not amplified in the patients can 15 be positively associated with a particular disease by further analysis. Alternatively, the PCR analysis may yield fragments of different lengths when the samples are derived from an individual having the phenotype associated with the disease than when the sample is derived from a healthy individual, indicating that the gene containing the extended cDNA may be responsible for the genetic disease.

VI. Use of Extended cDNAs (or genomic DNAs obtainable therefrom) to Construct Vectors

The present extended cDNAs (or genomic DNAs obtainable therefrom) may also be used to construct secretion vectors capable of directing the secretion of the proteins encoded by genes inserted in the vectors. Such secretion vectors may facilitate the purification or enrichment of the proteins encoded by genes inserted therein by reducing the number of background proteins from which the desired protein must be purified or enriched. Exemplary secretion vectors are described in Example 54 below.

25

30

20

EXAMPLE 54

Construction of Secretion Vectors

The secretion vectors of the present invention include a promoter capable of directing gene expression in the host cell, tissue, or organism of interest. Such promoters include the Rous Sarcoma Virus promoter, the SV40 promoter, the human cytomegalovirus promoter, and other promoters familiar to those skilled in the art.

A signal sequence from an extended cDNA (or genomic DNA obtainable therefrom), such as one of the signal sequences in SEQ ID NOs: 40-140 and 242-377 as defined in Table IV above, is operably linked to the promoter such that the mRNA transcribed from the promoter will direct the translation of the signal peptide. The host cell, tissue, or organism may be any cell, tissue, or organism which recognizes the signal peptide encoded by the signal sequence in the extended cDNA (or genomic DNA obtainable therefrom). Suitable hosts include mammalian cells, tissues or organisms, avian cells, tissues, or organisms, insect cells, tissues or organisms, or yeast.

In addition, the secretion vector contains cloning sites for inserting genes encoding the proteins which are to be secreted. The cloning sites facilitate the cloning of the insert gene in frame with the signal sequence such that a fusion protein in which the signal peptide is fused to the protein encoded by the inserted gene is expressed from the mRNA transcribed from the promoter. The signal peptide directs the extracellular secretion of the fusion protein.

The secretion vector may be DNA or RNA and may integrate into the chromosome of the host, be stably maintained as an extrachromosomal replicon in the host, be an artificial chromosome, or be transiently present in the host. Many nucleic acid backbones suitable for use as secretion vectors are known to those skilled in the art, including retroviral vectors, SV40 vectors, Bovine Papilloma Virus vectors, yeast integrating plasmids, yeast episomal plasmids, yeast artificial chromosomes, human artificial chromosomes, P element vectors, baculovirus vectors, or bacterial plasmids capable of being transiently introduced into the host.

The secretion vector may also contain a polyA signal such that the polyA signal is located downstream of the gene inserted into the secretion vector.

After the gene encoding the protein for which secretion is desired is inserted into the secretion vector, the secretion vector is introduced into the host cell, tissue, or organism using calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection, viral particles or as naked DNA. The protein encoded by the inserted gene is then purified or enriched from the supernatant using conventional techniques such as ammonium sulfate precipitation, immunoprecipitation, immunochromatography, size exclusion chromatography, ion exchange chromatography, and hplc. Alternatively, the secreted protein may be in a sufficiently enriched or pure state in the supernatant or growth media of the host to permit it to be used for its intended purpose without further enrichment.

The signal sequences may also be inserted into vectors designed for gene therapy. In such vectors, the signal sequence is operably linked to a promoter such that mRNA transcribed from the promoter encodes the signal peptide. A cloning site is located downstream of the signal sequence such that a gene encoding a protein whose secretion is desired may readily be inserted into the vector and fused to the signal sequence. The vector is introduced into an appropriate host cell. The protein expressed from the promoter is secreted extracellularly, thereby producing a therapeutic effect.

The extended cDNAs or 5' ESTs may also be used to clone sequences located upstream of the extended cDNAs or 5' ESTs which are capable of regulating gene expression, including promoter sequences, enhancer sequences, and other upstream sequences which influence transcription or translation levels. Once identified and cloned, these upstream regulatory sequences may be used in expression vectors designed to direct the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative fashion. Example 55 describes a method for cloning sequences upstream of the extended cDNAs or 5' ESTs.

Use of Extended cDNAs or 5' ESTs to Clone Upstream

Sequences from Genomic DNA

Sequences derived from extended cDNAs or 5' ESTs may be used to isolate the promoters of the corresponding genes using chromosome walking techniques. In one chromosome walking technique, which utilizes the 5 GenomeWalker™ kit available from Clontech, five complete genomic DNA samples are each digested with a different restriction enzyme which has a 6 base recognition site and leaves a blunt end. Following digestion, oligonucleotide adapters are ligated to each end of the resulting genomic DNA fragments.

For each of the five genomic DNA libraries, a first PCR reaction is performed according to the manufacturer's instructions using an outer adaptor primer provided in the kit and an outer gene specific primer. The gene specific primer 10 should be selected to be specific for the extended cDNA or 5' EST of interest and should have a melting temperature, length, and location in the extended cDNA or ' EST which is consistent with its use in PCR reactions. Each first PCR reaction contains 5ng of genomic DNA, 5 μ l of 10X Tth reaction buffer, 0.2 mM of each dNTP, 0.2 μ M each of outer adaptor primer and outer gene specific primer, 1.1 mM of Mg(OAc),, and 1 μ l of the Tth polymerase 50X mix in a total volume of 50 μ l. The reaction cycle for the first PCR reaction is as follows: 1 min @ 94°C / 2 sec @ 94°C, 3 min @ 15 72°C (7 cycles) / 2 sec @ 94°C, 3 min @ 67°C (32 cycles) / 5 min @ 67°C.

The product of the first PCR reaction is diluted and used as a template for a second PCR reaction according to the manufacturer's instructions using a pair of nested primers which are located internally on the amplicon resulting from the first PCR reaction. For example, 5 µl of the reaction product of the first PCR reaction mixture may be diluted 180 times. Reactions are made in a 50 μ l volume having a composition identical to that of the first PCR reaction except 20 the nested primers are used. The first nested primer is specific for the adaptor, and is provided with the GenomeWalker™ kit. The second nested primer is specific for the particular extended cDNA or 5' EST for which the promoter is to be cloned and should have a melting temperature, length, and location in the extended cDNA or 5' EST which is consistent with its use in PCR reactions. The reaction parameters of the second PCR reaction are as follows: 1 min @ 94°C / 2 sec @ 94°C, 3 min @ 72°C (6 cycles) / 2 sec @ 94°C, 3 min @ 67°C (25 cycles) / 5 min @ 67°C

The product of the second PCR reaction is purified, cloned, and sequenced using standard techniques. Alternatively, two or more human genomic DNA libraries can be constructed by using two or more restriction enzymes. The digested genomic DNA is cloned into vectors which can be converted into single stranded, circular, or linear DNA. A biotinylated oligonucleotide comprising at least 15 nucleotides from the extended cDNA or 5' EST sequence is hybridized to the single stranded DNA. Hybrids between the biotinylated oligonucleotide and the single stranded DNA containing 30 the extended cDNA or EST sequence are isolated as described in Example 29 above. Thereafter, the single stranded DNA containing the extended cDNA or EST sequence is released from the beads and converted into double stranded DNA using a primer specific for the extended cDNA or 5' EST sequence or a primer corresponding to a sequence included in the cloning vector. The resulting double stranded DNA is transformed into bacteria. DNAs containing the 5' EST or extended cDNA sequences are identified by colony PCR or colony hybridization.

Once the upstream genomic sequences have been cloned and sequenced as described above, prospective promoters and transcription start sites within the upstream sequences may be identified by comparing the sequences upstream of the extended cDNAs or 5' ESTs with databases containing known transcription start sites, transcription factor binding sites, or promoter sequences.

5 In addition, promoters in the upstream sequences may be identified using promoter reporter vectors as described in Example 56.

EXAMPLE 56

Identification of Promoters in Cloned Upstream Sequences

The genomic sequences upstream of the extended cDNAs or 5' ESTs are cloned into a suitable promoter 10 reporter vector, such as the pSEAP-Basic, pSEAP-Enhancer, pSgal-Basic, pSgal-Enhancer, or pEGFP-1 Promoter Reporter vectors available from Clontech. Briefly, each of these promoter reporter vectors include multiple cloning sites positioned upstream of a reporter gene encoding a readily assayable protein such as secreted alkaline phosphatase, β galactosidase, or green fluorescent protein. The sequences upstream of the extended cDNAs or 5' ESTs are inserted into the cloning sites upstream of the reporter gene in both orientations and introduced into an appropriate host cell. The 15 level of reporter protein is assayed and compared to the level obtained from a vector which lacks an insert in the cloning site. The presence of an elevated expression level in the vector containing the insert with respect to the control vector indicates the presence of a promoter in the insert. If necessary, the upstream sequences can be cloned into vectors which contain an enhancer for augmenting transcription levels from weak promoter sequences. A significant level of expression above that observed with the vector lacking an insert indicates that a promoter sequence is present in the 20 inserted upstream sequence.

Appropriate host cells for the promoter reporter vectors may be chosen based on the results of the above described determination of expression patterns of the extended cDNAs and ESTs. For example, if the expression pattern analysis indicates that the mRNA corresponding to a particular extended cDNA or 5' EST is expressed in fibroblasts, the promoter reporter vector may be introduced into a human fibroblast cell line.

Promoter sequences within the upstream genomic DNA may be further defined by constructing nested deletions in the upstream DNA using conventional techniques such as Exonuclease III digestion. The resulting deletion fragments can be inserted into the promoter reporter vector to determine whether the deletion has reduced or obliterated promoter activity. In this way, the boundaries of the promoters may be defined. If desired, potential individual regulatory sites within the promoter may be identified using site directed mutagenesis or linker scanning to obliterate 30 potential transcription factor binding sites within the promoter individually or in combination. The effects of these mutations on transcription levels may be determined by inserting the mutations into the cloning sites in the promoter reporter vectors.

EXAMPLE 57

Cloning and Identification of Promoters

Using the method described in Example 55 above with 5' ESTs, sequences upstream of several genes were obtained. Using the primer pairs GGG AAG ATG GAG ATA GTA TTG CCT G (SEQ ID NO:29) and CTG CCA TGT ACA TGA TAG AGA GAT TC (SEQ ID NO:30), the promoter having the internal designation P13H2 (SEQ ID NO:31) was obtained.

Using the primer pairs GTA CCA GGGG ACT GTG ACC ATT GC (SEQ ID NO:32) and CTG TGA CCA TTG CTC CCA AGA GAG (SEQ ID NO:33), the promoter having the internal designation P15B4 (SEQ ID NO:34) was obtained.

Using the primer pairs CTG GGA TGG AAG GCA CGG TA (SEQ ID NO:35) and GAG ACC ACA CAG CTA GAC AA (SEQ ID NO:36), the promoter having the internal designation P2986 (SEQ ID NO:37) was obtained.

Figure 8 provides a schematic description of the promoters isolated and the way they are assembled with the corresponding 5' tags. The upstream sequences were screened for the presence of motifs resembling transcription factor binding sites or known transcription start sites using the computer program Matinspector release 2.0, August 1996.

Figure 9 describes the transcription factor binding sites present in each of these promoters. The columns labeled matrice provides the name of the Matinspector matrix used. The column labeled position provides the 5' postion of the promoter site. Numeration of the sequence starts from the transcription site as determined by matching the genomic sequence with the 5' EST sequence. The column labeled "orientation" indicates the DNA strand on which the site is found, with the + strand being the coding strand as determined by matching the genomic sequence with the sequence of the 5' EST. The column labeled "score" provides the Matinspector score found for this site. The column labeled "length" provides the length of the site in nucleotides. The column labeled "sequence" provides the sequence of the site found.

The promoters and other regulatory sequences located upstream of the extended cDNAs or 5' ESTs may be used to design expression vectors capable of directing the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative manner. A promoter capable of directing the desired spatial, temporal, developmental, and quantitative patterns may be selected using the results of the expression analysis described in Example 26 above. For example, if a promoter which confers a high level of expression in muscle is desired, the promoter sequence upstream of an extended cDNA or 5' EST derived from an mRNA which is expressed at a high level in muscle, as determined by the method of Example 26, may be used in the expression vector.

Preferably, the desired promoter is placed near multiple restriction sites to facilitate the cloning of the desired insert downstream of the promoter, such that the promoter is able to drive expression of the inserted gene. The promoter may be inserted in conventional nucleic acid backbones designed for extrachromosomal replication, integration into the host chromosomes or transient expression. Suitable backbones for the present expression vectors include retroviral backbones, backbones from eukaryotic episomes such as SV40 or Bovine Papilloma Virus, backbones from bacterial episomes, or artificial chromosomes.

WO 99/31236 PCT/IB98/02122

.82.

Preferably, the expression vectors also include a polyA signal downstream of the multiple restriction sites for directing the polyadenylation of mRNA transcribed from the gene inserted into the expression vector.

Following the identification of promoter sequences using the procedures of Examples 55-57, proteins which interact with the promoter may be identified as described in Example 58 below.

5

Part Com

30

EXAMPLE 58

Identification of Proteins Which Interact with Promoter Sequences, Upstream

Regulatory Sequences, or mRNA

Sequences within the promoter region which are likely to bind transcription factors may be identified by homology to known transcription factor binding sites or through conventional mutagenesis or deletion analyses of reporter plasmids containing the promoter sequence. For example, deletions may be made in a reporter plasmid containing the promoter sequence of interest operably linked to an assayable reporter gene. The reporter plasmids carrying various deletions within the promoter region are transfected into an appropriate host cell and the effects of the deletions on expression levels is assassed. Transcription factor binding sites within the regions in which deletions reduce expression levels may be further localized using site directed mutagenesis, linker scanning analysis, or other techniques familiar to those skilled in the art. Nucleic acids encoding proteins which interact with sequences in the promoter may be identified using one-hybrid systems such as those described in the manual accompanying the Matchmaker One-Hybrid System kit available from Clontech (Catalog No. K1603-1). Briefly, the Matchmaker One-hybrid system is used as follows. The target sequence for which it is desired to identify binding proteins is cloned upstream of a selectable reporter gene and integrated into the yeast genome. Preferably, multiple copies of the target sequences are inserted into the reporter plasmid in tandem.

A library comprised of fusions between cDNAs to be evaluated for the ability to bind to the promoter and the activation domain of a yeast transcription factor, such as GAL4, is transformed into the yeast strain containing the integrated reporter sequence. The yeast are plated on selective media to select cells expressing the selectable marker linked to the promoter sequence. The colonies which grow on the selective media contain genes encoding proteins which bind the target sequence. The inserts in the genes encoding the fusion proteins are further characterized by sequencing. In addition, the inserts may be inserted into expression vectors or in vitro transcription vectors. Binding of the polypeptides encoded by the inserts to the promoter DNA may be confirmed by techniques familiar to those skilled in the art, such as gel shift analysis or DNAse protection analysis.

VII. Use of Extended cDNAs (or Genomic DNAs Obtainable Therefrom) in Gene Therapy

The present invention also comprises the use of extended cDNAs (or genomic DNAs obtainable therefrom) in gene therapy strategies, including antisense and triple helix strategies as described in Examples 57 and 58 below. In antisense approaches, nucleic acid sequences complementary to an mRNA are hybridized to the mRNA intracellularly, thereby blocking the expression of the protein encoded by the mRNA. The antisense sequences may prevent gene expression through a variety of mechanisms. For example, the antisense sequences may inhibit the ability of ribosomes

to translate the mRNA. Alternatively, the antisense sequences may block transport of the mRNA from the nucleus to the cytoplasm, thereby limiting the amount of mRNA available for translation. Another mechanism through which antisense sequences may inhibit gene expression is by interfering with mRNA splicing. In yet another strategy, the antisense nucleic acid may be incorporated in a ribozyme capable of specifically cleaving the target mRNA.

5

EXAMPLE 59

Preparation and Use of Antisense Oligonucleotides

The antisense nucleic acid molecules to be used in gene therapy may be either DNA or RNA sequences. They may comprise a sequence complementary to the sequence of the extended cDNA (or genomic DNA obtainable therefrom). The antisense nucleic acids should have a length and melting temperature sufficient to permit formation of an intracellular duplex having sufficient stability to inhibit the expression of the mRNA in the duplex. Strategies for designing antisense nucleic acids suitable for use in gene therapy are disclosed in Green et al., Ann. Rev. Biochem. 55:569-597 (1986) and Izant and Weintraub, Cell 36:1007-1015 (1984).

In some strategies, antisense molecules are obtained from a nucleotide sequence encoding a protein by reversing the orientation of the coding region with respect to a promoter so as to transcribe the opposite strand from that which is normally transcribed in the cell. The antisense molecules may be transcribed using in vitro transcription systems such as those which employ T7 or SP6 polymerase to generate the transcript. Another approach involves transcription of the antisense nucleic acids in vivo by operably linking DNA containing the antisense sequence to a promoter in an expression vector.

Alternatively, ofigonucleotides which are complementary to the strand normally transcribed in the cell may be synthesized in vitro. Thus, the antisense nucleic acids are complementary to the corresponding mRNA and are capable of hybridizing to the mRNA to create a duplex. In some embodiments, the antisense sequences may contain modified sugar phosphate backbones to increase stability and make them less sensitive to RNase activity. Examples of modifications suitable for use in antisense strategies are described by Rossi et al., Pharmacol. Ther. 50(2):245-254, (1991).

Various types of antisense oligonucleotides complementary to the sequence of the extended cDNA (or genomic DNA obtainable therefrom) may be used. In one preferred embodiment, stable and semi-stable antisense oligonucleotides described in International Application No. PCT W094/23026 are used. In these molecules, the 3' end or both the 3' and 5' ends are engaged in intramolecular hydrogen bonding between complementary base pairs. These molecules are better able to withstand exonuclease attacks and exhibit increased stability compared to conventional antisense oligonucleotides.

In another preferred embodiment, the antisense oligodeoxynucleotides against herpes simplex virus types 1 and 2 described in International Application No. WO 95/04141.

In yet another preferred embodiment, the covalently cross-linked antisense oligonucleotides described in International Application No. WO 96/31523 are used. These double- or single-stranded oligonucleotides comprise one or WO 99/31236 PCT/IB98/02122

.84

more, respectively, inter- or intra-oligonucleotide covalent cross-linkages, wherein the linkage consists of an amide bond between a primary amine group of one strand and a carboxyl group of the other strand or of the same strand, respectively, the primary amine group being directly substituted in the 2' position of the strand nucleotide monosaccharide ring, and the carboxyl group being carried by an aliphatic spacer group substituted on a nucleotide or nucleotide analog of the other strand or the same strand, respectively.

The antisense oligodeoxynucleotides and oligonucleotides disclosed in International Application No. WO
92/18522 may also be used. These molecules are stable to degradation and contain at least one transcription control
recognition sequence which binds to control proteins and are effective as decoys therefor. These molecules may contain
"hairpin" structures, "dumbbell" structures, "modified dumbbell" structures, "cross-linked" decoy structures and "loop"

10 structures.

In another preferred embodiment, the cyclic double-stranded oligonucleotides described in European Patent Application No. 0 572 287 A2 are used. These ligated oligonucleotide "dumbbells" contain the binding site for a transcription factor and inhibit expression of the gene under control of the transcription factor by sequestering the factor.

15

Use of the closed antisense oligonucleotides disclosed in International Application No. WO 92/19732 is also contemplated. Because these molecules have no free ends, they are more resistant to degradation by exonucleases than are conventional oligonucleotides. These oligonucleotides may be multifunctional, interacting with several regions which are not adjacent to the target mRNA.

The appropriate level of antisense nucleic acids required to inhibit gene expression may be determined using in vitro expression analysis. The antisense molecule may be introduced into the cells by diffusion, injection, infection or transfection using procedures known in the art. For example, the antisense nucleic acids can be introduced into the body as a bare or naked oligonucleotide, oligonucleotide encapsulated in lipid, oligonucleotide sequence encapsidated by viral protein, or as an oligonucleotide operably linked to a promoter contained in an expression vector. The expression vector may be any of a variety of expression vectors known in the art, including retroviral or viral vectors, vectors capable of extrachromosomal replication, or integrating vectors. The vectors may be DNA or RNA.

The antisense molecules are introduced onto cell samples at a number of different concentrations preferably between 1x10⁻¹⁰M to 1x10⁻⁴M. Once the minimum concentration that can adequately control gene expression is identified, the optimized dose is translated into a dosage suitable for use in vivo. For example, an inhibiting concentration in culture of 1x10⁻⁷ translates into a dose of approximately 0.6 mg/kg bodyweight. Levels of oligonucleotide approaching 100 mg/kg bodyweight or higher may be possible after testing the toxicity of the oligonucleotide in laboratory animals. It is additionally contemplated that cells from the vertebrate are removed, treated with the antisense oligonucleotide, and reintroduced into the vertebrate.

It is further contemplated that the antisense oligonucleotide sequence is incorporated into a ribozyme sequence to enable the antisense to specifically bind and cleave its target mRNA. For technical applications of ribozyme and antisense oligonucleotides see Rossi et al., supra.

In a preferred application of this invention, the polypeptide encoded by the gene is first identified, so that the

effectiveness of antisense inhibition on translation can be monitored using techniques that include but are not limited to
antibody-mediated tests such as RIAs and ELISA, functional assays, or radiolabeling.

The extended cDNAs of the present invention (or genomic DNAs obtainable therefrom) may also be used in gene therapy approaches based on intracellular triple helix formation. Triple helix oligonucleotides are used to inhibit transcription from a genome. They are particularly useful for studying alterations in cell activity as it is associated with a particular gene. The extended cDNAs (or genomic DNAs obtainable therefrom) of the present invention or, more preferably, a portion of those sequences, can be used to inhibit gene expression in individuals having diseases associated with expression of a particular gene. Similarly, a portion of the extended cDNA (or genomic DNA obtainable therefrom) can be used to study the effect of inhibiting transcription of a particular gene within a cell. Traditionally, homopurine sequences were considered the most useful for triple helix strategies. However, homopyrimidine sequences can also inhibit gene expression. Such homopyrimidine oligonucleotides bind to the major groove at homopurine:homopyrimidine sequences. Thus, both types of sequences from the extended cDNA or from the gene corresponding to the extended cDNA are contemplated within the scope of this invention.

EXAMPLE 60

Preparation and use of Triple Helix Probes

The sequences of the extended cDNAs (or genomic DNAs obtainable therefrom) are scanned to identify 10-mer to 20-mer homopyrimidine or homopurine stretches which could be used in triple-helix based strategies for inhibiting gene expression. Following identification of candidate homopyrimidine or homopurine stretches, their efficiency in inhibiting gene expression is assessed by introducing varying amounts of oligonucleotides containing the candidate sequences into tissue culture cells which normally express the target gene. The oligonucleotides may be prepared on an oligonucleotide synthesizer or they may be purchased commercially from a company specializing in custom oligonucleotide synthesis, such as GENSET, Paris, France.

The oligonucleotides may be introduced into the cells using a variety of methods known to those skilled in the art, including but not limited to calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection or native uptake.

Treated cells are monitored for altered cell function or reduced gene expression using techniques such as

Northern blotting, RNase protection assays, or PCR based strategies to monitor the transcription levels of the target
gene in cells which have been treated with the oligonucleotide. The cell functions to be monitored are predicted based
upon the homologies of the target gene corresponding to the extended cDNA from which the oligonucleotide was derived
with known gene sequences that have been associated with a particular function. The cell functions can also be

predicted based on the presence of abnormal physiologies within cells derived from individuals with a particular inherited disease, particularly when the extended cDNA is associated with the disease using techniques described in Example 53.

The oligonucleotides which are effective in inhibiting gene expression in tissue culture cells may then be introduced in vivo using the techniques described above and in Example 59 at a dosage calculated based on the in vitro results, as described in Example 59.

In some embodiments, the natural (beta) anomers of the oligonucleotide units can be replaced with alpha anomers to render the oligonucleotide more resistant to nucleases. Further, an intercalating agent such as ethicium bromide, or the like, can be attached to the 3' end of the alpha oligonucleotide to stabilize the triple helix. For information on the generation of oligonucleotides suitable for triple helix formation see Griffin et al. (Science 245:967-10 971 (1989).

EXAMPLE 61

Use of Extended cDNAs to Express an Encoded Protein in a Host Organism

The extended cDNAs of the present invention may also be used to express an encoded protein in a host organism to produce a beneficial effect. In such procedures, the encoded protein may be transiently expressed in the host organism or stably expressed in the host organism. The encoded protein may have any of the activities described above. The encoded protein may be a protein which the host organism lacks or, alternatively, the encoded protein may augment the existing levels of the protein in the host organism.

A full length extended cDNA encoding the signal peptide and the mature protein, or an extended cDNA encoding only the mature protein is introduced into the host organism. The extended cDNA may be introduced into the host organism using a variety of techniques known to those of skill in the art. For example, the extended cDNA may be injected into the host organism as naked DNA such that the encoded protein is expressed in the host organism, thereby producing a beneficial effect.

Alternatively, the extended cDNA may be cloned into an expression vector downstream of a promoter which is active in the host organism. The expression vector may be any of the expression vectors designed for use in gene therapy, including viral or retroviral vectors.

The expression vector may be directly introduced into the host organism such that the encoded protein is expressed in the host organism to produce a beneficial effect. In another approach, the expression vector may be introduced into cells in vitro. Cells containing the expression vector are thereafter selected and introduced into the host organism, where they express the encoded protein to produce a beneficial effect.

EXAMPLE 62

Use Of Signal Peptides Encoded By 5' Ests Or Sequences

Obtained Therefrom To Import Proteins Into Cells

The short core hydrophobic region (h) of signal peptides encoded by the 5'ESTS or extended cDNAs derived from the 5'ESTs of the present invention may also be used as a carrier to import a peptide or a protein of interest, so-

called cargo, into tissue culture cells (Lin et al., J. Biol. Chem., 270: 14225-14258 (1995); Du et al., J. Peptide Res., 51: 235-243 (1998); Rojas et al., Nature Biotech., 16: 370-375 (1998)).

When cell permeable peptides of limited size (approximately up to 25 amino acids) are to be translocated across cell membrane, chemical synthesis may be used in order to add the hiregion to either the C-terminus or the N-terminus to the cargo peptide of interest. Alternatively, when longer peptides or proteins are to be imported into cells, nucleic acids can be genetically engineered, using techniques familiar to those skilled in the art, in order to link the extended cDNA sequence encoding the hiregion to the 5' or the 3' end of a DNA sequence coding for a cargo polypeptide. Such genetically engineered nucleic acids are then translated either in vitro or in vivo after transfection into appropriate cells, using conventional techniques to produce the resulting cell permeable polypeptide. Suitable hosts cells are then simply incubated with the cell permeable polypeptide which is then translocated across the membrane.

This method may be applied to study diverse intracellular functions and cellular processes. For instance, it has been used to probe functionally relevant domains of intracellular proteins and to examine protein-protein interactions involved in signal transduction pathways (Lin et al., supra; Lin et al., J. Biol. Chem., 271: 5305-5308 (1996); Rojas et al., J. Biol. Chem., 271: 27456-27461 (1996); Liu et al., Proc. Netl. Acad. Sci. USA, 93: 11819-11824 (1996); Rojas et al., Bioch. Biophys. Res. Commun., 234: 675-680 (1997)).

Such techniques may be used in cellular therapy to import proteins producing therapeutic effects. For instance, cells isolated from a patient may be treated with imported therapeutic proteins and then re-introduced into the wave order or host organism.

Alternatively, the h region of signal peptides of the present invention could be used in combination with a nuclear localization signal to deliver nucleic acids into cell nucleus. Such digonucleotides may be antisense oligonucleotides or oligonucleotides designed to form triple helixes, as described in examples 59 and 60 respectively, in order to inhibit processing and maturation of a target cellular RNA.

EXAMPLE 63

Reassembling & Resequencing of Clones

Full length cDNA clones obtained by the procedure described in Example 27 were double-sequenced. These sequences were assembled and the resulting consensus sequences were then reanalyzed. Open reading frames were reassigned following essentially the same process as the one described in Example 27.

After this reanalysis process a few abnormalities were revealed. The sequences presented in SEO ID NOs: 47, 73, 79, 89, 91, 96, 126, 128, 134, and 139 are apparently unlikely to be genuine full length cDNAs. These clones are missing a stop codon and are thus more probably 3' truncated cDNA sequences. Similarly, the sequences presented in SEO ID NOs: 45, 50, 54, 57, 73, 74, 89, 92, 95, 98, 126, 129, 130, 131 and 139 may also not be genuine full length cDNAs based on homology studies with existing protein sequences. Although both of these sequences encode a potential start methionine each could represent a 5' truncated cDNA.

In addition, SEQ ID NO: 115 was found to be an alternatively spliced transcript and the identities of some of the bases in SEQ ID NO: 131 were corrected.

Finally, after the reassignment of open reading frames for the clones, new open reading frames were chosen in some instances. For example, in the case of SEQ ID NOs: 41, 47, 50, 52, 54-56, 58, 59, 61, 74, 75, 79, 84, 89, 91, 92, 96, 98, 103, 105, 106, 126, 129, 131, and 133 the new open reading frames were no longer predicted to contain a signal peptide.

As discussed above, Table IV provides the sequence identification numbers of the extended cDNAs of the present invention, the locations of the full coding sequences in SEQ ID NOs: 40-140 and 242-377 (i.e. the nucleotides encoding both the signal peptide and the mature protein, listed under the heading FCS location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the signal peptides (listed under the heading SigPep Location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the mature proteins generated by cleavage of the signal peptides (listed under the heading Mature Polypeptide Location in Table IV), the locations in SEQ ID NOs: 40-140 and 242-377 of stop codons (listed under the heading Stop Codon Location in Table IV) the locations in SEQ ID NOs: 40-140 and 242-377 of polyA signals (listed under the heading g PolyA Signal Location in Table IV) and the locations of polyA sites (listed under the heading PolyA Site Location in Table IV).

As discussed above, Table V lists the sequence identification numbers of the polypeptides of SEQ ID NOs: 141-241 and 378-513, the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the full length polypeptide (second column), the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the signal peptides (third column), and the locations of the amino acid residues of SEQ ID NOs: 141-241 and 379-513 in the mature polypeptide created by cleaving the signal peptide from the fall length polypeptide (fourth column). In Table V, and in the appended sequence listing, the first amino acid of the mature protein resulting from cleavage of the signal peptide is designated as amino acid number 1 and the first amino acid of the signal peptide is designated with the appropriate negative number, in accordance with the regulations governing sequence listings.

25

EXAMPLE 64

Functional Analysis of Predicted Protein Sequences

Following double-sequencing, new contigs were assembled for each of the extended cDNAs of the present invention and each was compared to known sequences available at the time of filing. These sequences originate from the following databases: Genbank (release 108 and daily releases up to October, 15, 1998), Genseq (release 32) PIR (release 33) and SwissProt (release 35). The predicted proteins of the present invention matching known proteins were further classified into 3 categories depending on the level of homology.

The first category contains proteins of the present invention exhibiting more than 70% identical amino acid residues on the whole length of the matched protein. They are clearly close homologues which most probably have the same function or a very similar function as the matched protein.

The second category contains proteins of the present invention exhibiting more remote homologies (40 to 70% over the whole protein) indicating that the protein of the present inventionmay have functions similar to those of the homologous protein.

The third category contains proteins exhibiting homology (90 to 100%) to a domain of a known protein indicating that the matched protein and the protein of the invention may share similar features.

It should be noted that the numbering of amino acids in the protein sequences discussed in Figures 10 to 15, and Table VIII, the first methicanine encountered is designated as amino acid number 1. In the appended sequence listing, the first amino acid of the mature protein resulting from cleavage of the signal peptide is designated as amino acid number 1, and the first amino acid of the signal peptide is designated with the appropriate negative number, in accordance with the regulations governing sequence listings.

In addition all of the corrected amino acid sequences (SEQ ED NOs: 141-241 and 378-513) were scanned for the presence of known protein signatures and motifs. This search was performed agains, the Prosite 15.0 database, using the Proscan software from the GCG package- Functional signatures and their locations are indicated in Table VIII.

15 A) Proteins which are closely related to known proteins

Protein of SEQ ID NO: 217

20

....The protein of SEQ ID NO: 217 encoded by the extended cDNA SEQ ID NO: 116 isolated from lymphocyte shows complete identity to a human protein TFAR19 that may play a role in apoptosis (Genbank accession number AF014955, SEQ ID NO: 516) as shown by the alignment in figure 10.

Taken together, these data suggest that the protein of SEQ ID NO: 217 may be involved in the control of development and homeostasis. Thus, this protein may be useful in diagnosis and/or treating several types of disorders including, but not limited to, cancer, autoimmune disorders, viral infections such as AIDS, neurodegenerative disorders, osteoporosis.

25 Proteins of SEQ ID NOs: 174, 175 and 232

The proteins of SEQ ID NOs: 174, 175 and 232 encoded by the extended cDNAs SEQ ID NOs:. 73, 74 and 131 respectively and isolated from lymphocytes shows complete extensive homologies to a human secreted protein (Genseq accession number W36955, SEQ ID NO: 517). As shown by the alignments of figure 11, the amino acid residues are identical to those of the 110 amino acid long matched protein except for positions 51 and 108-110 of the matched protein for the protein of SEQ ID NOs: 174, for positions 48, 94 and 108-110 of the matched protein of SEQ ID NOs:175 and for positions 94, and 108-110 of the matched protein for the protein of SEQ ID NOs: 232. Proteins of SEQ ID NOs: 174 and 232 may represent alternative forms issued from alternative use of polyadenylation signals.

Taken together, these data suggest that the proteins of SEQ IO NOs: 174, 175 and 232 may play a role in cell proliferation and/or differentiation, in immune responses and/or in haematopoesis. Thus, this protein or part therein,

may be useful in diagnosing and treating several disorders including, but not limited to, cancer, immunological, haematological and/or inflammatory disorders. It may also be useful in modulating the immune and inflammatory responses to infectious agents and/or to suppress graft rejection.

5 Proteins of SEQ ID NO: 231

The protein of SEQ ID NO: 231 encoded by the extended cDNA SEQ ID NO: 130 shows extensive homology with the human E25 protein (Genbank accession number AF038953, SEQ ID NO: 515). As shown by the alignments in figure 12, the amino acid residues are identical except for position 159 in the 263 amino acid long matched sequence. The matched protein might be involved in the development and differentiation of haematopoietic stem/progenitor cells.

In addition, it is the human homologue of a murine protein thought to be involved in chondro-osteogenic differentiation and belonging to a novel multigene family of integral membrane proteins (Deleersnijder et al, J. Biol. Chem., 271: 19475-19482 (1996)).

The protein of invention contains two short segments from positions 1 to 21 and from 100 to 120 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10 : 685-686 (1994)). The first transmembrane domains matches exactly those predicted for the murine E25 protein.

Taken together, these data suggest that the protein of SEQ ID NO: 231 may be involved in cellular proliferation and differentiation. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer and embryogenesis disorders.

20 Protein of SEQ ID NO: 196

The protein of SEQ ID NO: 196 encoded by the extended cDNA SEQ ID NO: 95 shows extensive homology with the human seventransmembrane protein (Genbank accession number Y11395, SEQ ID NO: 518) and its murine homologue (Genbank accession number Y11550). As shown by the alignments in figure 13, the amino acid residues are identical except for position 174 in the 399 amino acid long human matched sequence. The matched protein potentially associated to stomatin may act as a G-protein coupled receptor and is likely to be important for the signal transduction in neurons and haematopoietic cells (Mayer et al, Biochem. Biophys. Acta., 1395 : 301-308 (1998)).

Taken together, these data suggest that the protein of SEO ID NOs: 196 may be involved in signal transduction. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases cardiovascular disorders, hypertension, renal injury and repair and septic 30 shock.

Protein of SEQ ID NO: 158

The protein of SEQ ID NOs: 158 encoded by the extended cDNA SEQ ID NO: 57 shows homology with the murine subunit 7a of the COP9 complex (Genbank accession number AF071316, SEQ ID NO: 520). As shown by the

alignments in figure 14, the amino acid residues are identical except for positions 90, 172 and 247 in the 275 amino acid long matched sequence. This complex is highly conserved between mammals and higher plants where it has been shown to act as a repressor of photomorphogenesis All the components of the mammalian COP9 complex contain structural features also present in components of the proteasome regulatory complex and the translation initiation complex eIF3 complex, suggesting that the mammalian COP9 complex is an important cellular regulator modulating multiple signaling pathways (Wei et al, Curr. Biol., 8 : 919-922 (1998)).

Taken together, these data suggest that the protein of SEQ ID NO: 158 may be involved in cellular signaling, probably as a subunit of the human COP9 complex. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, cardiovascular disorders, hypertension, renal injury and repair and septic shock.

Protein of SEQ ID NO: 226

The protein of SEQ ID NO: 226 encoded by the extended cDNA SEQ ID NO: 125 shows homology with the bovine subunit B14.5B of the NADH-ubiquinone oxidureductase complex (Arizmendi et al., FEBS Lett., 313: 80-84 (1992) and Swissprot accession -number Q02827, SEQ ID NO: 514). As shown by the alignments in figure 15, the amino acid residues are identical except for positions 3-4, 6-12, 32-34, 47, 53-55, 67 and 69-74 in the 120 amino acid residues are identical except for positions 3-4, 6-12, 32-34, 47, 53-55, 67 and 69-74 in the 120 amino acid residues. This complex is the first of four complexes located in the inner mitochondrial membrane and composing the mitochondrial electron transport chain. Complex I is involved in the dehydrogenation of NADH and the transportation of electrons to coenzyme Q. It is composed of 7 subunits encoded by the mitochondrial genome and 34 subunits encoded by the nuclear genome. It is also thought to play a role in the regulation of apoptosis and necrosis. Mitochondriocytopathies due to complex I deficiency are frequently encountered and affect tissues with a high energy demand such as brain (mental retardation, convulsions, movement disorders), heart (cardiomyopathy, conduction disorders), kidney (Fanconi syndrome), skeletal muscle (exercise intolerance, muscle weakness, hypotonia) and/or eye (opthmaloplegia, ptosis, cataract and retinopathy). For a review on complex I see Smeitink et al., Hum. Mol. Gent., 7: 1573-1579 (1998).

Taken together, these data suggest that the protein of SEQ ID NO: 226 may be part of the mitochondrial energy-generating system, probably as a subunit of the NADH-ubiquinone oxidoreductase complex. Thus, this protein or part therein, may be useful in diagnosing and/or treating several disorders including, but not limited to, brain disorders (mental retardation, convulsions, movement disorders), 'heart disorders (cardiomyopathy, conduction disorders), kidney disorders (Fanconi syndrome), skeletal muscle disorders (exercise intolerance, muscle weakness, hypotonia) and/or eye disorders opthmalmoplegia, ptosis, cataract and retinopathy).

B) Proteins which are remotely related to proteins with known functions

<u>Proteins of SEO ID NOs:</u> 149, 150 and 211

The proteins of SEQ ID NOs: 1.49,150 and 211 encoded by the extended cDNAs SEQ ID NOs: 48, 49 and 110 respectively and found in, skeletal muscle shows homologies with T1/ST2 ligand polypeptide of either human (Genbank accession number U41804 and Genseq accession number W09639) or rodent species (Genbank accession number U41805 and Genseq accession number W09640). These polypeptides are thought to be cytokines that bind to the ST2 receptor, a member of the immunoglobulin family homologous to the interleukin-1 receptor and present on some lymphoma cells. They are predicted to be cell-surface proteins containing a short transmembrane domain. (Gayle et al, J. Biol. Chem., 271: 5784-5789 (1996)). Proteins of SEQ ID NOs: 149, 150 and 211 may represent alternative forms issued from alternative use of polyadenylation signals.

The protein of invention contains two short transmembrane segments from positions 5 to 25 and from 195 to 215 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, **10**:685-686 (1994)). The second transmembrane domain matches exactly those of the matched cell-surface protein.

Taken together, these data suggest that the protein of SEQ ID NOs: 149, 150 and 211 may act as a cytokine, thus may play a role in the regulation of cell growth and differentiation and/or in the regulation of the immune response.

Thus, this protein or part therein, may be useful in diagnosing and treating several disorders including, but not limited to, cancer, immunological, haematological and/or inflammatory disorders. It may also be useful in modulating the immune and inflammatory responses to infectious agents such as HIV and/or to suppress graft rejection.

reund is a patric

Protein of SEQ ID NO: 177

ta one - equiple

The protein SEQ ID NO: 177 found in testis encoded by the extended cDNA SEQ ID NO: 76 shows homologies to serine protease inhibitor proteins belonging to the pancreatic trypsin inhibitor family (Kunitz) such as the extracellular proteinase inhibitor named chelonianin (Swissprot accession number P00993). The characteristic PROSITE signature of this family is conserved in the protein of the invention (positions 69 to 87) except for a drastic change of the last cysteine residue into an arginine residue.

Taken together, these data suggest that the protein of SEQ ID NO: 177 may be a protease inhibitor, probably

of the Kunitz family. Thus, this protein or part therein, may be useful in diagnosing and treating several disorders
including but not limited to, cancer and neurodegenerative disorders such as Alzheimer's disease.

Protein of SEQ ID NO: 146

The protein SEQ ID NO: 146 encoded by the extended cDNA SEQ ID NO: 45 shows homology to human apolipoprotein L (Genbank accession number AF019225). The matched protein is a secreted high density lipoprotein associated with apoA-I-containing lipoproteins which play a key role in reverse cholesterol transport.

Taken together, these data suggest that the protein of SEO ID NO 146 may play a role in lipid metabolism. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to,

hyperlipidemia, hypercholesterolemia, atherosclerosis, cardiovascular disorders such as, coronary heart disease, and neurodegenerative disorders such as Alzheimer's disease or dementia.

Protein of SEQ-ID NO: 163

The protein SEQ ED NO: 163 encoded by the extended cDNA SEQ ID NO: 62 shows homology to the yeast autophagocytosis protein AUT1 (SwissProt accession number P40344). The matched protein is required for starvation-induced non-specific bulk transport of cytoplasmic proteins to the vacuole.

Taken together, these data suggest that the protein of SEQ ID NO: 163 may play a role in protein transport.

Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to,
autoimmune disorders and immune disorders due to dysfunction of antigen presentation.

C) Proteins homologous to a domain of a protein with known function

Protein of SEQ ID NO: 214

The protein of SEQ ID NO: 214 encoded by the extended cDNA SEQ ID NO: 113 and expressed in adult brain shows extensive homology to part of the murine SHYC protein (Genbank accession number AF072897) which is expressed in the developing and embryonic nervous system as well as along the olfactory pathway in adult brains (Köster et al., Neuroscience Letters., 252::69-71;(1998)).

Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system

| Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the protein of SEQ ID NO: 214 may play a role in nervous system
| Taken together, the prote

Protein of SEQ ID NO: 225

The protein of SEO ID NO: 225 encoded by the extended cDNA SEO ID NO: 124 and expressed in adult prostate belong to the phosphatidylethanolainin-binding protein from which it exhibits the characteristic PROSITE signature from positions 90 to 112 (see table VIII). Proteins from this widespread family, from nematodes to fly, yeast, rodent and primate species, bind hydrophobic ligands such as phospholipids and nucleotides. They are mostly expressed in brain and in testis and are thought to play a role in cell growth and/or maturation, in regulation of the sperm maturation, motility and 'in membrane remodeling. They may act either through signal transduction or through oxidoreduction reactions (for a review see Schoentgen and Jollès, FEBS Letters, 369: 22-26 (1995)).

Taken together, these data suggest that the protein of SEQ ID NO: 225 may play a role in cell. Thus, these growth, maturation and in membrane remodeling and/or may be related to male fertility. Thus, this protein may be useful in diagnosing and/or treating cancer, neurodegenerative diseases, and/of, disorders related to male fertility and sterility.

Protein of SEQ ID NO: 153

30

The protein of SEQ ID NO: 153 encoded by the extended cDNA SEQ ID NO. 52 and expressed in brain exhibits homology to different integral membrane proteins. These membrane proteins include the nematode protein SRE-2 (Swissprot accession number Q09273) that belongs to the multigene SRE family of *C. elegans* receptor-like proteins and a family of tricarboxylate carriers conserved between flies and mammals. One member of this matched family is the rat tricarboxylate carrier (Genbank accession number S70011), an anion transporter localized in the inner membrane of mitochondria and involved in the biosynthesis of fatty acids and cholesterol. The protein of the invention contains a short transmembrane segments from positions 5 to 25 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10:685-686 (1994)).

Taken together, these data suggest that the protein of SEQ ID NO: 153 may play a role in signal transduction and/or in molecule transport. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, immune disorders, cardiovascular disorders, hypertension, renal injury and repair and septic shock

Protein of SEQ ID NO: 213

15

20

25

The protein of SEQ ID NO: 213 encoded by the extended cDNA SEQ ID NO: 112 and expressed in brain exhibits homology with part of the tRNA pseudouridine 55 synthase found in *Escherichia Coli* (Swissprot accession number P09171). This bacterial protein belongs to the NAP57/CBF5/TRUB family of nucleolar proteins found in bacteria, yeasts and mammals involved in rRNA or tRNA biosynthesis, ribosomal subunit assembly and/or centromere/mircotubule binding.

Taken together, these data suggest that the protein of SEQ ID NO: 213 may play a role in rRNA or tRNA biogensis and function. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, hearing loss or disorders linked to chromosomal instability such as dyskeratosis.

Protein of SEQ ED NO: 240

The protein of SEQ ID NO: 240 encoded by the extended cDNA SEQ ID NO: 139 and expressed in brain exhibits homology with a family of eukaryotic cell surface antigens containing 4 transmembrane domains. The PROSITE signature for this family is conserved in the protein of the invention except for a substitution of an alanine residue in place of any of the following hydrophic residues: leucine, valine, isoleucine or methionine (positions 21 to 36).

The protein of the invention contains three short transmembrane segments from positions 6 to 26, 32 to 52

30 and from 56 to 76 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10: 685-686 (1994)). These transmembrane domains match the last three transmembrane domains of the matched protein family.

Taken together, these data suggest that the protein of SEO ID NO: 240 may play a role in immunological and/or inflammatory responses, probably as a cell surface antigen. Thus, this protein or part therein, may be useful in diagnosing and treating several disorders including, but not limited to, cancer, immunological, haematological and/or

inflammatory disorders. It may also be useful in modulating the immune and inflammatory responses to infectious agents and/or to suppress graft rejection.

Protein of SEQ ID NO: 239

5

10

20

The protein of SEQ ID NO: 239 encoded by the extended cDNA SEQ ID NO: 138 exhibits homology with a conserved region in a family of NA+/H+ exchanger conserved in yeast, nematode and mammals. These cation/proton exchangers are integral membrane proteins with 5 transmembrane segments involved in intracellular pH regulation, maintenance of cell volume, reabsorption of sodium across specialized epithelia, vectorial transport and are also thought to play a role in signal transduction and especially in the induction of cell proliferation and in the induction of apoptosis.

The protein of invention contains four short transmembrane segments from positions 21 to 41, 48 to 68 and from 131 to 151 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10: 685-686 (1994)). The third and fourth transmembrane domains match the fourth and fifth transmembrane segments of the matched family of proteins.

Taken together, these data suggest that the protein of SEQ ID NO: 239 may play a role in membrane

15 permeability and/or in signal transduction. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, cardiovascular disorders, hypertension, renal injury and repair, septic shock as well as disorders of membrane permeability such as diarrhea.

ារតែការ ២០ irsed in ១៩៤

Protein of SEQ ID NO: 200

The protein of SEQ ID NO: 200 encoded by the extended cDNA SEQ ED NO: 99 and expressed in brain exhibits extensive homology to the N-terminus of cell division cycle protein 23 (Genbank accession number AF053977) and also

to a lesser extent to its homologue in Saccharomyces carevisiae. The matched protein is required for chromosome segregation and is part of the anaphae-promoting complex necessary for cell cycle progression to mitosis.

Taken together, these data suggest that the protein of SEQ ID NO: 200 may play a role in cellular mitosis.

Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer and leukemia.

Protein of SEQ ID NO: 230

The protein of SEQ ID NO: 230 encoded by the extended cDNA SEQ ID NO: 129 exhibits extensive homology to the C-terminus of the eta subunit of T-complex polypeptide 1 conserved from yeasts to mammals, and even complete identity with the last 54 amino acid residues of the human protein (Genbank accession number AF026292). The matched protein is a chaperonin which assists the folding of actins and tubulins in eukaryotic cells upon ATP hydrolysis.

Taken together, these data suggest that the protein of SEQ ID NO: 230 may play a role in the folding, transport, assembly and degradation of proteins. Thus, this protein may be useful in diagnosing and/or treating several

types of disorders including, but not limited to, cancer, cardiovascular disorders, immune disorders, neurodegenerative disorders, osteoporosis and arthritis.

Protein of SEQ ED NO: 167

The protein of SEQ ID NO: 167 encoded by the extended cDNA SEQ ID NO: 66 exhibits homology to a monkey pepsinogen A-4 precursor (Swissprot accession number P27678) and to related members of the aspartyl protease family. The matched protein belongs to a family of widely distributed proteolytic enzymes known to exist in vertebrate, fungi, plants, retroviruses and some plant viruses.

Taken together, these data suggest that the protein of SEQ ID NO: 167 may play a role in the degradation of proteins. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, autoimmune disorders and immune disorders due to dysfunction of antigen presentation.

Protein of SEO ID NO: 179

The protein of SEQ ID NO: 179 encoded by the extended cDNA SEQ ID NO: 78 found in testis exhibits

homology to part of mammalian collipase precursors. Collipases are secreted cofactors for pancreatic lipases that allow the lipase to anchor at the water-lipid interface. Collipase plays a crucial role in the intestinal digestion and absorption of dietary fats. The 5 cysteines characteristic for this protein family are conserved in the protein of the invention although the collipase PROSITE signature is not.

Taken together, these data suggest that the protein of SEQ ED NO: 179 may play a role in the lipid metabolism and/or in male fertility. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, hyperlipidemia, hypercholesterolemia, atherosclerosis, cardiovascular disorders such as coronary heart disease, and neurodegenerative disorders such as Alzheimer's disease or dementia, and disorders linked to male fertility.

25 Protein of SEQ ID NO: 227

The protein of SEQ ID NO: 227 encoded by the extended cDNA SEQ ID NO: 126 exhibits extensive homology to the ATP binding region of a whole family of serine/threonine protein kinases belonging to the CDC2/CDC28 subfamily.

The PROSITE signature characteristic for this domain is present in the protein of the invention from positions 10 to 34.

Taken together, these data suggest that the protein of SEQ ED NO: 158 may bind ATP, and even be a protein 30 kinase. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, cardiovascular disorders, hypertension, renal injury and repair and septic shock.

WO 99/31236

5

Although this invention has been described in terms of certain preferred embodiments, other embodiments which will be apparent to those of ordinary skill in the art in view of the disclosure herein are also within the scope of this invention. Accordingly, the scope of the invention is intended to be defined only by reference to the appended claims.

.97.

PCT/IB98/02122

As discussed above, the extended cDNAs of the present invention or portions thereof can be used for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to 10 compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic (ingerprinting; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination for expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or 15 potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins or polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit 20 another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other 25 protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing 30 such methods include without limitation "Molecular Cloning; A Laboratory Manual", 2d ed., Cole Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology; Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a

nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

SEQUENCE LISTING FREE TEXT

The following free text appears in the accompanying Sequence Listing:

In vitro transcription product

oligonucleotide

5 promoter

transcription start site

Von Heijne matrix

Score

matinspector prediction

10 name

al Page

TABLE I

SEQ ID NO. in Present application	Provisional Application Disclosing Sequence	SEQ ID NO. in provisional application
40	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	51
41	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	72
42	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	52
43	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	78
44	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	73
45	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	41
46	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	67
47	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	82
48	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	80
49	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	81
50	U.S. Provisional Patent Application Serial No. 60/096, 116, filed Aug. 10, 1998	
51	U.S. Provisional Patent Application Serial No. 60/096, 116, filed Aug. 10, 1998	53
52		54
53	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	195
	U.S. Provisional Patent Application Serial No. 60/074, 121, filed Feb. 9, 1998	44
54	U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997	46
. 55	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	68
56	U.S. Provisional Patent Application Serial No. 60/074, 121, filed Feb. 9, 1998	48
57	U.S. Provisional Patent Application Serial No. 60/096, 116, filed Aug. 10, 1998	55
58	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	49
59	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	50
60	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	97
61	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	51
62	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	69
63	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	49
64	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	199
65	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	53
66	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	57
67	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	54
68	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	55
69	U.S. Provisional Patent Application Serial No. 60/096.116, filed Aug. 10, 1998	58
70	U.S. Provisional Patent Application Serial No. 60/096.116, filed Aug. 10, 1998	59

CONT. TABLE !

	-
U.S. Provisional Patent Application Serial No. 60/096, 116, filed Aug. 10, 1998	60
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	112
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	52
U.S. Provisional Patent Application Serial No. 60/074, 121, filed Feb. 9, 1998	59
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	60
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	136
U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	75
U.S. Provisional Patent Application Serial No. 60/096, 116, filed Aug. 10, 1998	61
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	61
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	130
U.S. Provisional Patent Application Serial No. 60/096, 116, filed Aug. 10, 1998	65
U.S. Provisional Patent Application Serial No. 60/069,957, füed Dec. 17, 1997	54
U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	78
U.S. Provisional Patent Application Serial No. 60/074, 121, filed Feb. 9, 1998	63
U.S. Provisional Patent Application Serial No. 60/074, 121, filed Feb. 9, 1998	65
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	152
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	66
U.S. Provisional Patent Application Serial No. 60/074, 121, filed Feb. 9, 1998	67
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	60
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	68
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	61
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	62
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	166
U.S. Provisional Patent Application Sarial No. 60/074,121, filed Feb. 9, 1998	70
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	73
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	63
U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	52
U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	62
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	176
U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	63
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	187
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	190
U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	83
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	180
U.S. Provisional Patent Application Serial No. 60/096, 116, filed Aug. 10, 1998	64
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	69
	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998 U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998 U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998 U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998 U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998 U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998 U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998 U.S. Provisional Patent Application Serial No. 60/098,116, filed Aug. 10, 1998 U.S. Provisional Patent Application Serial No. 60/098,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/098,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998 U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998 U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998 U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998 U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998 U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997 U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997

CO	NIT	T	A	o		1
LU	N		×	ы	LE.	

CONT. TABLE I		
· 107	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	40
108	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	77
109	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	43
110	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	82
111	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	76
112	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	43
113	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	46
114	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	47
115	U.S. Provisional Patent Application Serial No. 60/066,677, filed Nov. 13, 1997	53
116	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	58
117	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	74
118	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	71
119	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	145
120	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	67
121	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	58
122	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	72
123	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	73
124	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	70
125	U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997	40
126	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	44
127	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	45
128	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	47
129	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	48
130	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	51
131	U.S. Provisional Patent Application Serial No. 60/066,677, filed Nov. 13, 1997	50
132	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	56
133	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	57
134	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	71
135	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	72
136	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	64
137	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	65
138	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	66
139	U.S. Provisional Patent Application Serial No. 60/069.957 filed Dec. 17, 1997	74
140	U.S. Provisional Patent Application Serial No. 60/096.116 filed Aug. 10, 1998	67
242	U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997	75
243	U.S. Provisional Patent Application Serial No. 60:069,957, filled Dec. 17, 1997	76

CONT. TABLE I		
244	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	77
245	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	78
246	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	79
247	U.S. Provisional Patent Application Serial No. 60/069,957, tiled Dec. 17, 1997	80
248	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	81
249	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	82
250	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	83
251	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	84
252	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	85
253	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	86
254	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	87
255	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	88
256	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	89
257	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	90
258	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	91
259	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	92
260	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	93
261	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	94
262	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	95
263	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	96
264	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	97
265	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	98
266	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	99
267	U.S. Provisional Patent Application Serial No. 60(069,957, filed Dec. 17, 1997	100
268	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	101
269	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	102
270	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	103
271	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	104
` 272	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	105
273	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	106
274	U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997	107
275	U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997	108
276	U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997	109
277	U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997	110
278	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	111
279	U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997	112

280 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 113 281 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 114 282 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 115 283 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 116 284 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 117 285 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 118 286 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 119 287 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 120	5
282 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 115 283 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 116 284 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 117 285 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 118 286 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 119 287 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 120	5
283 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 116 284 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 117 285 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 118 286 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 119 287 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 120	i
284 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 117 285 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 118 286 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 119 287 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 120	
285 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 118 286 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 119 287 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 120	1
286 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 119 287 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 120	
287 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 120]
)
288 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	
290 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 123	3
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	1
292 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 125	i
293 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 126	3
294 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 127	,
295 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 128	}
296 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 129)
297 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 130)
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	
299 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 132	2
300 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 133	3
301 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 134	ļ
302 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 135	;
303 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 136	3
304 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 137	,
305 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 138	3
306 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 139	3
307 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997) <u> </u>
308 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 14	1
309 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 14	2
310 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 14	3
311 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 14	4
312 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 14	5
313 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 14	6
314 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 14	7
315 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 14	8

U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 149	CONT. TABLE I		
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 151	316	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	149
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 152 153 152 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 153 153 155	317	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	150
320 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 153 321 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 154 322 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 155 323 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 155 324 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 157 325 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 158 326 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 169 327 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 160 328 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 162 329 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 163 330 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 163 331 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 164 332 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 165 333 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 165 333 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 166 334 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 168 335 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 170 336 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 171 337 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 172 340 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 172 341 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 172 342 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 173 343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 174 345 U.S. Provisional Patent Application Seria	318	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	151
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 154	319	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	152
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 155	320	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	153
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 156 324 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 157 325 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 158 326 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 159 327 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 160 328 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 161 329 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 162 330 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 163 331 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 164 332 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 165 333 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 166 334 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 167 335 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 168 334 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 168 335 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 169 337 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 170 338 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 171 339 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 172 340 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 173 341 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 174 342 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 175 343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 176 344	321	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	154
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 157 158 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 158 159	322	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	155
U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 159 150 159 159 159 159 159 150 159 159 150 159 159 150 159 159 150 159 159 150 159 159 150 159 159 150 159 159 150 159 159 159 150 159 1	323	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	156
U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 159 160 150 1	324	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	157
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 160	325	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	158
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 162	326	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	159
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 163	327	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	160
330 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 163 331 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 164 332 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 165 333 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 166 334 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 167 335 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 168 336 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 169 337 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 170 338 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 171 339 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 172 340 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 173 341 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 174 342 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 175 343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 175 344 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 176 345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 179 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 179 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180	328	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	161
331 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 165 332 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 165 333 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 166 334 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 167 335 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 168 336 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 169 337 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 170 338 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 171 339 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 172 340 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 173 341 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 174 342 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 175 343 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 175 344 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 176 345 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 176 346 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 179 347 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 179 348 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 180 349 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 181	329	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	162
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 165	330	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	163
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 166	331	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	164
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 168	332	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	165
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 168	333	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	166
336 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 170	334	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	167
337 U.S. Provisional Patent Application Serial No. 60/069,957, filed Oec. 17, 1997 170 338 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 171 339 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 172 340 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 173 341 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 174 342 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 175 343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 176 344 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 177 345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	335	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	168
338 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 171 339 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 172 340 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 173 341 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 174 342 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 175 343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 176 344 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 177 345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	336	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	169
339 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 172 340 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 173 341 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 174 342 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 175 343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 176 344 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 177 345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 180 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 181 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dac. 17, 1997 183	337	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	170
340 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 173 341 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 174 342 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 175 343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 176 344 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 177 345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 179 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	338	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	171
341 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 174 342 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 175 343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 176 344 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 177 345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 179 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	339	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	172
342 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 175 343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 176 344 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 177 345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 179 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	340	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	173
343 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 176 344 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 177 345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 179 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	341	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	174
344 U.S. Provisional Patent Application Serial No. 60/069,957, filed Oac. 17, 1997 177 345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 179 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	342	U.S. Provisional Patent Application Serial No. 60/069,957, filed Oec. 17, 1997	175
345 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 178 346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 179 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	343	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	176
346 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 179 347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	344	U.S. Provisional Patent Application Serial No. 60/069,957, filed Oec. 17, 1997	177
347 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 180 348 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	345	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	178
348 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 181 349 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997 183	346	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	179
349 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 182 350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	347	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	180
350 U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997 183	348	U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997	181
	349	U.S. Provisional Patent Application Serial No. 60/069.957, filed Dec. 17, 1997	182
	350	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	183
	351	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	184

CONT. TABLE I

CUNT. TABLE I		<u> </u>
352	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	185
353	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	186
354	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	187
355	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	188
356	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	189
357	U.S. Provisional Patent Application Serial No. 60(069,957, filed Dec. 17, 1997	190
358	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	191
359	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	192
360	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	193
361	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	194
362	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	195
363	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	196
364	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	197
365	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	1998
366	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	199
367	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	200
368	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	201
369	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	202
370	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	203
371	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	204
372	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	205
373	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	206
374	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	207
375	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	208
376	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	209
377	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	210

TABLE II: Parameters used for each step of EST analysis

		Search Charac	teristics	Selection Charac	teristics
Step	Program	Strand	Parameters	Identity (%))	Length (bp)
Miscellaneous	Blastn	both	S-61 X-16	90	17
tRNA	Fasta	both		80	60
rRNA	Blastn	both	S=108	80	40
mtRNA	Blastn	both	S = 108	80	40
Procaryotic	Blastn	both	S-144	90	40
Fungal	Blastn	both	S=144	90	40
Alu	fasta*	both	•	70	40
L1	Blastn	both	S-72	70	40
Repeats	Blastn	both	S=72	70	40
Promoters	Blastn	top	S-54 X-16	90	15⊥
Vertebrate	fasta*	both	S-108	90	30
ESTs	Blatsn	both	S-108 X-16	90	30
Proteins	blastxn	top	E = 0.001		

[&]quot; use "Quick Fast" Database Scanner

 $[\]pm$ alignment further constrained to begin closer than 10bp to EST\5' and 5 $\,\eta$ using BLOSUM62 substitution matrix

TABLE III: Parameters used for each step of extended cDNA analysis

Search characteristics			Selection characteristics				
Step	Program	Strand	Parameters	Identity (%)	Length (bp)	Comments	
miscellaneous •	FASTA	beth	·	90	15		
tRNA1	FASTA	beth		80	90	 	
rRNA'	BLASTN	both	S-108	80	40		
mtRNA'	BLASTN	both	S-108	80	40	 	
Procaryotic ¹	BLASTN	both	S-144	90	40	 	
Fungai*	BLASTN	both	S-144	90	40	 	
Alu*	BLASTN	both	S-72	70	40	max 5 matches, masking	
L1'	BLASTN	both	S-72	70	40	max 5 matches, masking	
Repeats*	BLASTN	both	S-72	70	40	masking	
PotyA	BLAST2N	tep	W-6.S-10.E-1000	90	8	in the last 20 nucleotides	
Polyadenylati on signal		top	AATAAA allowing 1 mis	match		in the 50 nucleatides preceding the 5' end of the palA	
Vertebrate*	BLASTN then FASTA	both		90 then 70	30	first BLASTN and then FASTA on matching sequences	
ESTs*	BLAST2N	both		90	30	33,33,33	
Geneseq	BLASTN	both	W-8, B-10	90	30		
ORF	BLASTP	top	W-8, 8-10			on ORF proteins, max 10 matches	
Proteins*	BLASTX	top	E=0.001	70	30		

^{*} steps common to EST analysis and using the same algorithms and parameters

5 * steps also used in EST analysis but with different algorithms and/or parameters

TABLE IV

id	FCS Location	SigPep Location	Mature Polypeptide Location	Stop Codon	PolyA Signal Location	PolyA Site Location
40	7 through 471	7 through 99	100 through 471	Location 472	537 through 542	554 through 568
41	168 through 332		168 through 332	333	557 through 562	334 mrough 500
42	51 through 251	51 through 110	111 through 251	252	849 through 854	882 through 895
43	20 through 613	20 through 82	83 through 613	614		ooz inrough das
44	12 through 416	12 through 86	87 through 416	417	425 through 430	445 through 458
45	276 through 1040	276 through 485	486 through 1040	1041		2024 through 2036
46	443 through 619	443 through 589	590 through 619	620		1267 through 1276
47	206 through 747		206 through 747			
48	36 through 521	36 through 104	105 through 521	522	528 through 533	548 through 561
49	36 through 395	36 through 104	105 through 395	396	599 through 604	619 through 632
50	21 through 41		21 through 41	42	328 through 333	357 through 370
51	35 through 631	35 through 160	161 through 631	632	901 through 906	979 through 994
52	271 through 399		271 through 399	400		
53	103 through 252	103 through 213	214 through 252	253		588 through 597
54	2 through 460	·	2 through 460	461	713 through 718	735 through 748
55	31 through 231		31 through 231	232	769 through 774	690 through 703
56	305 through 565	ļ	305 through 565	566	694 through 699	713 through 725
57	124 through 873	124 through 378	379 through 873	874	1673 through 1678	1694 through 1705
58	135 through 206		135 through 206	207	850 through 855	1056 through 1069
59	135 through 818		135 through 818	819	909 through 914	1071 through 1084
60	33 through 290	33 through 92	93 through 290	291		
61	485 through 616		485 through 616	617		669 through 682
62	54 through 995	54 through 227	228 through 995	996	1130 through 1135	1181 through 1191
63	657 through 923	657 through 896	897 through 923	924	957 through 962	974 through 1008
64	18 through 311	18 through 62	63 through 311	312		1.
65	151 through 426	151 through 258	259 through 426	427	505 through 510	527 through 538
66	10 through 1062	10 through 57	58 through 1062	1063	1710 through 1715	1735 through 1747
67	78 through 491	78 through 218	219 through 491	492	1652 through 1657	1673 through 1686
68	69 through 371	69 through 287	288 through 371	372	510 through 515	530 through 542
69	2 through 757	2 through 205	206 through 757	758		1160 through 1174
70	2 through 1051	2 through 205	206 through 1051	1052	1248 through 1253	1272 through 1285
71	2 through 1171	2 through 205	206 through 1171	1172	1368 through 1373	1386 through 1398
72	42 through 611	42 through 287	288 through 611	612	787 through 792	808 through 821
73	62 through 916	62 through 757	758 through 916			904 through 916
74	62 through 520		62 through 520	521	1124 through 1129	1141 through 1153
75	21 through 167		21 through 167	168		
76	22 through 318	22 through 93	94 through 318	319	497 through 502	516 through 526
77	8 through 292	8 through 118	119 through 292	293	317 through 322	339 through 352
78	16 through 378	16 through 84	85 through 378	379	502 through 507	522 through 542

CONT. TABLE IV

CON	T. TABLE IV					
79	57 through 233		57 through 233			·
80	83 through 340	83 through 124	125 through 340	341	573 through 578	607 through 660
81	47 through 541	47 through 220	221 through 541	542	1.	597 through 605
82	46 through 285	46 through 150	151 through 285	286	364 through 369	385 through 396
83	22 through 240	22 through 84	85 through 240	241	397 through 402	421 through 432
84	89 through 382		89 through 382	383		408 through 420
85	80 through 415	80 through 142	143 through 415	416	471 through 476	488 through 501
86	152 through 361	152 through 283	284 through 361	362		
87	32 through 307	32 through 70	71 through 307	308	1240 through 1245	1261 through 1272
88	114 through 734	114 through 239	240 through 734	735	768 through 773	793 through 804
89	199 through 802	·	199 through 802		780 through 785	791 through 802
90	38 through 1174	38 through 148	149 through 1174	1175	1452 through 1457	1478 through 1490
91	26 through 361		26 through 361	·		350 through 361
92	3 through 131	•	3 through 131	132		591 through 605
93	33 through 185	33 through 80	81 through 185	186	570 through 575	586 through 591
94	184 through 915	184 through 237	238 through 915	916	1119 through 1124	1139 through 1150
95	58 through 1116	58 through 159	160 through 1116	1117	1486 through 1491	1504 through 1513
96	327 through 417		327 through 417			404 through 417
97	63 through 398	63 through 206	207 through 398	399	1.	
98	2 through 163		2 through 163	164	488 through 493	511 through 522
99	13 through 465	13 through 75	76 through 465	466		
100	20 through 703	20 through 94	95 through 703	704	1000 through 1005	1023 through 1041
101	103 through 294	103 through 243	244 through 294	295		
102	81 through 518	81 through 173	174 through 518	519		
103	66 through 326	•	66 through 326	327	1066 through 1071	1087 through 1098
104	170 through 289	170 through 250	251 through 289	290		†· —
105	36 through 497		36 through 497	498	650 through 655	663 through 685
106	18 through 320		18 through 320	321	539 through 544	542 through 554
107	71 through 1438	71 through 136	137 through 1438	1439	1644 through 1649	1665 through 1678
108	25 through 318	25 through 75	76 through 318	319	452 through 457	482 through 494
109	84 through 332	84 through 170	171 through 332	333	<u> - </u>	702 through 714
110	32 through 718	32 through 100	101 through 718	719	770 through 775	793 through 805
111	26 through 481	26 through 88	89 through 481	482	755 through 760	775 through 787
112	26 through 562	26 through 187	188 through 562	563	<u> </u>	· ·
113	4 through 810	4 through 279	280 through 810	811	858 through 863	881 through 893
114	55 through 459	55 through 120	121 through 459	460	1444 through 1449	1462 through 1475
115	48 through 248	48 through 161	162 through 248	249	283 through 288	308 through 321
116	25 through 399	25 through 186	187 through 399	400		
117	10 through 1137	10 through 72	73 through 1137	1138	1144 through 1149	1162 through 1173
118	72 through 704	72 through 161	162 through 704	705	772 through 777	
119	44 through 505	44 through 223	224 through 505	506		
120	25 through 393	25 through 150	151 through 393	394	734 through 739	757 through 770
	1			1	_1	

WO 99/31236 PCT/IB98/02122

-111-

CONT. TABLE IV

	I. LABLE IV					
121	58 through 1095	58 through 114	115 through 1095	1096	[·	1202 through 1213
122	31 through 660	31 through 90	91 through 660	661	1288 through 1293	1307 through 1318
123	31 through 582	31 through 90	91 through 582	583	816 through 821	840 through 853
124	15 through 695	15 through 80	81 through 695	696	795 through 800	814 through 826
125	74 through 295	74 through 196	197 through 295	296	545 through 550	561 through 571
126	440 through 659		440 through 659		601 through 606	
127	38 through 283	38 through 85	86 through 283	284	257 through 262	
128	121 through 477	121 through 288	289 through 477		·	
129	2 through 163	- 1	2 through 163	164	292 through 297	310 through 323
130	46 through 675	46 through 87	88 through 675	676	1364 through 1369	1383 through 1392
131	62.through 385	•	62 through 385	386	974 through 979	987 through 999
132	422 through 550	422 through 475	476 through 550	551		714 through 725
133	124 through 231	•	124 through 231	232		387 through 400
134	131 through 1053	131 through 169	170 through 1053		1019 through 1024	
135	86 through 403	86 through 181	182 through 403	404	1097 through 1102	1117 through 1128
136	37 through 162	37 through 93	94 through 162	163	224 through 229 .	243 through 254
137	31 through 381	31 through 90	91 through 381	382		875 through 886
138	46 through 579	46 through 156	157 through 579	580	·	
139	92 through 471	92 through 172	173 through 471		454 through 459	458 through 471
140	154 through 675	154 through 498	499 through 675	676	819 through 824	838 through 849
242	18 through 173	18 through 77	78 through 173	174	864 through 869	882 through 893
243	17 through 595	17 through 85	86 through 595	596	820 through 825	840 through 851
244	89 through 334	89 through 130	131 through 334	335	462 through 467	484 through 495
245	21 through 614	21 through 83	84 through 614	615	849 through 854	873 through 884
246	94 through 573	94 through 258	259 through 573	574	862 through 867	886 through 897
247	74 through 397	74 through 127	128 through 397	398	472 through 477	507 through 518
248	51 through 242	51 through 116	117 through 242	243	319 through 324	.339 through 350
249	111 through 191	111 through 155	156 through 191	192	965 through 970	986 through 996
250	45 through 602	45 through 107	108 through 602	603	828 through 833	850 through 860
251	24 through 560	24 through 101	102 through 560	561	563 through 568	583 through 593
252	109 through 558	109 through 273	274 through 558	559		1104 through 1114
253	128 through 835	128 through 220	221 through 835	836	1145 through 1150	1170 through 1181
254	59 through 505	59 through 358	359 through 505	506	1042 through 1047	1062 through 1073
255	1 through 207	1 through 147	148 through 207	208	784 through 789	807 through 818
256	12 through 734	12 through 101	182 through 734	.735	914 through 919	961 through 971
257	378 through 518	378 through 467	468 through 518	519	607 through 612	628 through 640
258	110 through 304	110 through 193	194 through 304	305	708 through 713	732 through 743
259	201 through 419	201 through 272	273 through 419	420	601 through 606	627 through 637
260	123 through 302	123 through 176	177 through 302	303	1279 through 1284	1301 through 1312
261	98 through 673	98 through 376	377 through 673	674		1025 through 1035
	17 through 463	17 through 232	233 through 463	464	657 through 662	684 through 696
262	17 131104911 403	•				

CONT. TABLE IV

	IT. TABLE IV					
264	42 through 299	42 through 101	102 through 299	300	·	762 through 775
265	198 through 431	198 through 260	261 through 431	432		1064 through 1074
266	279 through 473	279 through 362	363 through 473	474	944 1hrough 949	970 through 981
267	12 through 644	12 through 92	93 through 644	645	1002 through 1007	1020 through 1031
268	91 through 459	91 through 330	331 through 459	460		1271 through 1281
269	70 through 327	70 through 147	148 through 327	328	1741 through 1746	1763 through 1774
270	12 through 497	12 through 104	105 through 497	498	935 through 940	955 through 967
271	90 through 383	90 through 200	201 through 383	384	609 through 614	632 through 643
272	332 through 541	332 through 376	377 through 541	542	739 through 744	761 through 773
273	43 through 222	43 through 177	178 through 222	223	530 through 535	555 through 566
274	115 through 231	115 through 180	181 through 231	232	419 through 424	445 through 455
275	232 through 384	232 through 300	301 through 384	385	650 through 655	662 through 673
276	143 through 427	143 through 286	287 through 427	428	606 through 611	628 through 639
277	284 through 463	294 through 379	380 through 463	464	ļ	762 through 772
278	162 through 671	162 through 398	399 through 671	672	805 through 810	830 through 840
279	63 through 632	63 through 308	309 through 632	633	808 through 813	829 through 840
280	21 through 362	21 through 200	201 through 362	363	821 through 826	838 through 849
281	21 through 503	21 through 344	345 through 503	504	1305 through 1310	1330 through 1341
282	1 through 201	1 through 63	64 through 201	202	637 through 642	660 through 671
283	39 through 1034	39 through 134	135 through 1034	1035	1566 through 1571	1587 through 1597
284	69 through 263	69 through 125	126 through 263	264	1173 through 1178	1196 through 1205
285	115 through 285	115 through 204	205 through 285	286	505 through 510	525 through 536
286	90 through 344	90 through 140	141 through 344	345	500 through 505	515 through 527
287	57 through 311	57 through 107	108 through 311	312	467 through 472	482 through 493
288	96 through 302	96 through 182	183 through 302	303		501 through 514
289	161 through 526	161 through 328	329 through 526	527	·	799 through 811
290	210 through 332	210 through 299	300 through 332	333	594 through 599	613 through 625
291	212 through 361	212 through 319	320 through 361	362	650 through 655	673 through 684
292	75 through 482	75 through 128	129 through 482	483	595 through 600	618 through 627
293	50 through 631	50 through 244	245 through 631	632	777 through 782	801 through 812
294	154 through 576	154 through 360	361 through 576	577	737 through 742	763 through 775
295	154 through 897	154 through 360	361 through 897	898	1817 through 1022	1044 through 1054
296	146 through 292	146 through 253	254 through 292	293	395 through 400	433 through 444
297	126 through 383	126 through 167	168 through 383 .	384	726 through 731	743 through 754
298	66 through 497	66 through 239	240 through 497	498	594 through 599	618 through 629
299	49 through 411	49 through 96	97 through 411	412	732 through 737	750 through 763
300	49 through 534	49 through 96	97 through 534	535	593 through 598	612 through 623
301	86 through 415	86 through 145	146 through 415	416	540 through 545	560 through 571
302	56 through 268	56 through 100	101 through 268	269	584 through 589	601 through 612
303	32 through 328	32 through 103	104 through 328	329	508 through 513	528 through 539
304	21 through 527	21 through 95	96 through 527	528	921 through 926	953 through 963
305	147 through 647	147 through 374	375 through 647	648		668 through 681

CONT. TABLE IV

CU.						
306		262 through 306	307 through 471	472	663 through 668	682 through 693
307		74 through 172	173 through 1216	1217	1627 through 1632	1640 through 1652
308		48 through 89	90 through 164	165	482 through 487	505 through 517
309		185 through 295	296 through 334	335	355 through 360	392 through 405
310	195 through 347	195 through 272	273 through 347	348	1037 through 1042	1071 through 1082
311	90 through 815	90 through 179	180 through 815	816	883 through 888	905 through 916
312	52 through 513	52 through 231	232 through 513	514	553 through 558	572 through 583
313	172 through 438	172 through 354	355 through 438	439	682 through 687	885 through 697
314	148 through 366	148 through 225	226 through 366	367	770 through 775	792 through 803
315	175 through 336	175 through 276	277 through 336	337	•	812 through 823
316	191 through 553	191 through 304	305 through 553	554	765 through 771	804 through 817
317	106 through 603	106 through 216	217 through 603	604	•	1102 through 1112
318	47 through 586	47 through 124	125 through 586	587	1583 through 1588	1614 through 1623
319	99 through 371	99 through 290	291 through 371	372	491 through 496	513 through 524
320	44 through 814	44 through 112	113 through 814	815		978 through 989
321	3 through 581	3 through 182	183 through 581	582	·	1006 through 1016
322	107 through 427	107 through 190	191 through 427	428	499 through 504	516 through 529
323	45 through 407	45 through 83	84 through 407	408	1008 through 1013	1032 through 1042
324	201 through 332	201 through 251	252 through 332	333		869 through 880
325	217 through 543	217 through 255	256 through 543	544		1206 through 1217
326	18 through 446	18 through 140	141 through 446	447	930 through 935	948 through 959
327	29 through 724	29 through 118	119 through 724	725	886 through 891	910 through 920
328	404 through 586	404 through 466	467 through 586	587	1304 through 1309	1334 through 1344
329	331 through 432	331 through 387	388 through 432	433	548 through 553	573 through 585
330	59 through 703	59 through 220	221 through 703	704	886 through 891	903 through 914
331	672 through 752	872 through 722	723 through 752	753		1150 through 1161
332	57 through 311	57 through 128	129 through 311	312	332 through 337	351 through 363
333	80 through 232	80 through 127	128 through 232	233	617 through 622	634 through 645
334	91 through 291	91 through 219	220 through 291	292	367 through 372	389 through 400
335	196 through 384	196 through 240	241 through 384	385	461 through 466	485 through 496
336	54 through 590	54 through 227	228 through 590	591		955 through 965
337	133 through 846	133 through 345	346 through 846	847		890 through 901
338	138 through 671	138 through 248	249 through 671	672	1319 through 1324	1338 through 1347
339	124 through 411	124 through 186	187 through 411	412	948 through 953	971 through 983
340	372 through 494	372 through 443	444 through 494	495	708 through 713	732 through 745
341	112 through 450	112 through 192	193 through 450	45:	1053 through 1058	1095 through 1106
342	117 through 866	117 through 170	171 through 865	367	1159 through 1164	1178 through 1190
343	13 through 465	13 through 75	76 through 465	466	1035 through 1040	1060 through 1070
344	2 through 718	2 through 76	77 through 718	715	170 through 1175	1203 through 1213
345	86 through 709	86 through 361	362 through 709	71 C	943 through 948	963 through 973
346	63 through 320	63 through 179	180 through 320	321	771 through 776	799 through 810
347	299 through 418	299 through 379	380 through 418	419	39 through 744	762 through 771
		+ · · · · · ·			23 (mosgn /44	. or an andt \\

CONT. TABLE IV

348	186 through 380	186 through 233	234 through 380	381	383 through 388	396 through 409
349	69 through 458	69 through 233	234 through 458	459	564 through 569	602 through 613
350	12 through 638	12 through 263	264 through 638	639	951 through 956	975 through 985
351	282 through 389	282 through 332	333 through 389	390	1413 through 1418	1437 through 1447
352	208 through 339	208 through 294	295 through 339	340	1.	1631 through 1641
353	69 through 557	69 through 224	225 through 557	558	849 through 854	870 through 883
354	134 through 325	134 through 274	275 through 325	326		718 through 729
355	78 through 731	78 through 227	228 through 731	732		1002 through 1013
356	46 through 693	46 through 90	91 through 693	694	937 through 942	962 through 973
357	126 through 527	126 through 182	183 through 527	528	834 through 839	856 through 867
358	66 through 320	66 through 113	114 through 320	321	490 through 495	508 through 519
359	73 through 948	73 through 159	160 through 948	949		1016 through 1028
360	69 through 434	69 through 236	237 through 434	435	419 through 424	441 through 452
361	628 through 804	628 through 711	712 through 804	805		864 through 875
362	70 through 366	70 through 108	109 through 366	367	496 through 501	521 through 531
363	70 through 366	70 through 108	109 through 366	367	·	1233 through 1244
364	111 through 434	111 through 185	.186 through 434	435		618 through 631
365	19 through 567	19 through 63	64 through 567	568	749 through 754	771 through 781
366	19 through 312	19 through 63	64 through 312	313	896 through 901	921 through 931
367	64 through 612	64 through 234	235 through 612	613		839 through 849
368	39 through 458	39 through 80	81 through 458	459	613 through 618	633 through 644
369	9 through 185	9 through 50	51 through 185	186		906 through 918
370	14 through 316	14 through 121	122 through 316	317	442 through 447	458 through 471
371	70 through 1092	70 through 234	235 through 1092	1093	1475 through 1480	1493 through 1504
372	274 through 597	274 through 399	400 through 597	598	731 through 736	754 through 765
373	230 through 469	230 through 307	308 through 469	470	1004 through 1009	1027 through 1040
374	72 through 545	72 through 203	204 through 545	546	· · · · ·	1151 through 1162
375	36 through 425	36 through 119	120 through 425	426	1215 through 1220	1240 through 1250
376	155 through 751	155 through 340	341 through 751	752	912 through 917	937 through 947
377	46 through 585	46 through 120	121 through 585	586	584 through 589	606 through 619

TABLE V

ld	Full Length Polypeptide	Signal Peptide Location	Mature Polypeptide Location
	Location		oilhehting rocation
141	-31 through 124	-31 through -1	1 through 124
142	1 through 55		1 through 55
143	-20 through 47	-20 through -1	1 through 47
144	-21 through 177	-21 through -1	1 through 177
145	-25 through 110	-25 through -1	1 through 110
146	-70 through 185	-70 through -1	1 through 185
147	-49 through 10	-49 through -1	1 through 10
148	1 through 180		1 through 180
149	-23 through 139	-23 through -1	1 through 139
150	-23 through 97	-23 through -1	1 through 97
151	1 through 7	· · ·	1 through 7
152	-42 through 157	-42 through -1	1 through 157
153	1 through 43		1 through 43
154	-37 through 13	-37 through -1	1 through 13
155	1 through 153	•	1 through 153
156	1 through 67	·	1 through 67
157	1 through 87		1 through 87
158	-85 through 165	-85 through -1	1 through 165
159	1 through 24	•	1 through 24
160	1 through 228		1 through 228
161	-20 through 66	-20 through -1	1 through 66
162	1 through 44		1 through 44
163	-58 through 256	-58 through -1	1 through 256
164	-80 through 9	-80 through -1	1 through 9
165	-15 through 83	-15 through -1	1 through 83
166	-36 through 56	-36 through -1	1 through 56
167	-16 through 335	-16 through -1	1 through 335
168	-47 through 91	-47 through -1	1 through 91
169	-73 through 28	-73 through -1	1 through 28
170	-68 through 184	-68 through -1	1 through 184
171	-68 through 282	-68 through -1	1 through 282
172	-68 through 322	-68 through -1	1 through 322
173	82 through 108	-82 through -1	1 through 108
174	232 through 53	-232 through -1	1 through 53
175	1 through 153		1 through 153
176	1 through 49		1 through 49
177	-24 through 75	-24 through -1	1 through 75
178	-37 through 58	-37 through -1	1 through 58
179	-23 through 98	-23 through -1	1 through 98
180	1 through 59		1 through 59
181	-14 through 72	-14 through -1	1 through 72
182	58 through 107	-58 through -1	1 through 107
183	-35 through 45	-35 through -1	1 through 45
184	-21 through 52	-21 through -1	1 through 52
185	1 through 98		1 through 98
186	-21 through 91	-21 through -1	1 through 91
187	-44 through 26	-44 through -1	1 through 26
188	-13 through 79	-13 through -1	1 through 79
189	-42 through 165	-42 through -1	1 through 165
190	1 through 201		1 through 201

CONT. TABLE V

191 37 through 342 37 through -1 1 through 342 1 through 112 1 through 112 1 through 123 1 through 13 1 through 13 1 through 25 1-16 through -1 1 through 35 1-16 through 25 1-18 through 25 1-18 through 26 1-18 through 27 1 through 319 34 through -1 1 through 319 1 through 319 34 through -1 1 through 319 1 through 310 1 through 320	CONT. TABL	.E V		
1992 1 through 112 1 through 113 1 through 43 1 through 43 1 through 43 1 through 43 1 through 35 1-6 through 25 1-8 through 2-1 1 through 35 1-8 through 2-1 1 through 3-1 1 through 6-4 1 through 1-1 1 through 6-4 1 through 1-1 1 thro	191	-37 through 342	-37 through -1	1 through 362
1933	192		·	
194	193			
195	194		-16 through -1	
196	195			
197	196			
198	197		O T THE GOLD TO	
199	198		-48 through .1	
200 21 through 130 21 through -1 1 through 130 201 25 through 203 25 through -1 1 through 130 202 47 through 17 47 through -1 1 through 175 203 33 through 115 33 through -1 1 through 175 204 1 through 87 1 through 87 1 through 87 1 through 87 205 27 through 13 27 through -1 1 through 154 1 through 154 207 1 through 154 1 through 154 1 through 154 207 1 through 164 208 -22 through 434 -22 through -1 1 through 101 208 -22 through 434 -22 through -1 1 through 434 209 -17 through 81 -17 through -1 1 through 81 210 -29 through 54 -29 through -1 1 through 81 211 -23 through 206 -23 through -1 1 through 206 212 -21 through 131 -21 through -1 1 through 206 213 through -1 1 through 206 214 -29 through 13 -21 through -1 1 through 161 214 -29 through 155 -54 through -1 1 through 125 -54 through -1 1 through 177 -22 through -1 1 through 177 -21 through -1 1 through 179 -21 through 179 -21 through 170 -21 through 170 -22 through -1 1	199		10 110 00011 1	
201 25 through 203 25 through 1 1 through 203 202 47 through 17 47 through 1 1 through 203 31 through 115 33 through 1 1 through 115 204 1 through 87 1 through 87 1 through 87 1 through 13 205 27 through 13 27 through 1 1 through 13 206 1 through 154 1 through 154 1 through 154 207 1 through 101 1 through 101 1 through 101 1 through 101 208 22 through 434 22 through 1 1 through 434 209 1.7 through 54 22 through 1 1 through 434 209 1.7 through 54 22 through 1 1 through 434 210 29 through 54 22 through 1 1 through 54 211 23 through 54 22 through 1 1 through 54 211 23 through 131 21 through 1 1 through 131 21 through 1 1 through 131 22 through 1 1 through 131 23 through 1 1 through 131 22 through 1 1 through 137 23 through 1 1 through 137 24 through 1 1 through 137 24 through 1 1 through 137 25 through 1 1 through 138 25 through 25 thro	200		-21 through -1	
202	201			
203	202			
204				
205 27 through 13 27 through -1 1 through 13 206 1 through 154 1 through 154 1 through 154 1 through 154 207 1 through 101 1 through 101 208 22 through 434 -22 through -1 1 through 434 209 -17 through 81 -17 through -1 1 through 434 209 -17 through 84 -29 through -1 1 through 54 211 -23 through 54 -29 through -1 1 through 54 211 -23 through 131 -21 through -1 1 through 206 221 -21 through 131 -21 through -1 1 through 206 -23 through -1 1 through 131 -21 through -1 1 through 131 -21 through 131 -21 through -1 1 through 131 -21 through -1 1 through 131 -21 through -1 1 through 132 -21 through 131 -22 through -1 1 through 125 -22 through 131 -22 through -1 1 through 177 -23 through -1 1 through 179 -24 through 131 -22 through -1 1 through 179 -24 through 131 -22 through -1 1 through 179 -24 through 355 -22 through 355 -22 through 355 -22 through 355 -22 through 34 -24 through -1 1 through 355 -22 through 34 -24 through -1 1 through 355 -22 through 327 -39 through -1 1 through 381 -22 through 327 -39 through -1 1 through 381 -22 through 327 -39 through -1 1 through 381 -22 through 327 -39 through -1 1 through 33 -22 through 33 -30 through -1 1 through 33 -30 through -1 1 through 36 -32 through 33 -33 through -1 1 through 36 -32 through 33 -33 through -1 1 through 36 -32 through 34 -30 through -1 1 through 36 -32 through 34 -30 through -1 1 through 36 -32 through 34 -30 through -1 1 through 36 -32 through 34 -30 through -1 1 through 36 -32 through 34 -30 through -1 1 through 36 -32 through 34 -30 through -1 1 through 36 -32 through 34 -30 through -1 1 through 36 -32 through 36 -32 through 36 -32 through 36 -32 through 37 -33 through -1 1 through 37				
206				
1			-27 (inough -)	
208 -22 through 434 -22 through -1 1 through 434 209 -17 through 81 -17 through -1 1 through 81 -17 through -1 1 through 81 -17 through -1 1 through 54 -29 through -1 1 through 54 -29 through -1 1 through 54 -21 through -1 1 through 206 -22 through -1 1 through 206 -22 through -1 1 through 206 -22 through -1 1 through 131 -21 through -1 1 through 131 -21 through -1 1 through 131 -21 through -1 1 through 131 -22 through -1 1 through 125 -22 through 177 -22 through -1 1 through 131 -22 through -1 1 through 132 -23 through -1 1 through 133 -22 through -1 1 through 327 -23 through 355 -21 through -1 1 through 355 -21 through -1 1 through 355 -22 through 355 -22 through -1 1 through 355 -22 through 364 -20 through -1 1 through 365 -22 through 364 -20 through -1 1 through 367 -22 through 377 -22 through 384 -20 through -1 1 through 377 -22 through 39 -20 through -1 1 through 39 -20 through -1 1 through 377 -22 through 39 -20 through -1 1 through 39 -20 through -1 1 through 30 -22 through 30			 	
209 17 through 81 17 through 1 1 through 81 210 29 through 54 29 through -1 1 through 84 211 23 through 206 23 through -1 1 through 206 212 21 through 131 21 through 13 1 through 125 214 92 through 177 92 through -1 1 through 177 215 22 through 113 22 through -1 1 through 177 215 22 through 113 22 through -1 1 through 177 216 38 through 29 38 through -1 1 through 179 217 54 through 355 21 through -1 1 through 355 219 30 through 181 30 through -1 1 through 355 219 30 through 181 30 through -1 1 through 181 220 60 through 94 60 through -1 1 through 94 221 42 through 31 42 through -1 1 through 327 223 20 through 93 20 through 190 20 through -1 1 through 327 224 20 through 180 20 through -1 1 through 327 224 20 through 180 20 through -1 1 through 327 225 22 through 25 22 through 25 22 through 25 22 through 25 22 through 33 41 through -1 1 through 33 227 1 through 33 41 through -1 1 through 33 227 1 through 33 41 through -1 1 through 33 227 1 through 33 41 through -1 1 through 33 228 -16 through 66 -16 through -1 1 through 33 228 -16 through 66 -16 through -1 1 through 66 -16 through -1 1 through 67 229 -56 through 63 -56 through -1 1 through 54 1 through 36 1 through 36 1 through 37 1 through 38 20 through 29 21 through 39 22 through -1 1 through 39 23 through 39 37 through 31 1 through 39 37 through 39 27 through -1 1 through 39 39 37 through 39 27 through -1 1 through 59 378 20 through 99 27 through -1 1 through 99 39 39 30 through 99 20 through -1 1 through 99 39 39 30 through 99 20 through -1 1 through 99 30 through 99 20 through 90 1 through 9			22 sheered 1	
210 -29 through 54 -29 through -1 1 through 54				
211				
212 -21 through 131 -21 through -1 1 through 131 213 -54 through 125 -54 through -1 1 through 125 214 -92 through 177 -92 through -1 1 through 177 215 -7 -22 through 113 -22 through -1 1 through 177 215 -7 -22 through 13 -22 through -1 1 through 177 216 -38 through 29 -38 through -1 1 through 113 216 -38 through 35 -38 through -1 1 through 113 217 -54 through 355 -21 through -1 1 through 355 218 -21 through 355 -21 through -1 1 through 355 219 -30 through 181 -30 through -1 1 through 181 220 -60 through 94 -60 through -1 1 through 94 221 -42 through 81 -42 through -1 1 through 81 222 -19 through 327 -19 through -1 1 through 327 223 -20 through 190 -20 through -1 1 through 190 224 -20 through 164 -20 through -1 1 through 164 225 -22 through 205 -22 through -1 1 through 164 226 -41 through 33 -43 through -1 1 through 205 228 -16 through 66 -16 through -1 1 through 33 227 1 through 66 -16 through -1 1 through 66 229 -56 through 65 -56 through -1 1 through 66 230 1 through 66 -16 through -1 1 through 67 231 -14 through 196 -14 through -1 1 through 68 233 -18 through 54 -18 through -1 1 through 54 231 -14 through 36 -16 through -1 1 through 54 232 1 through 108 -1 through 54 233 -18 through 25 -18 through -1 1 through 294 234 1 through 36 -16 through -1 1 through 294 235 -13 through 294 -13 through -1 1 through 294 236 -32 through 74 -32 through -1 1 through 74 237 -19 through 23 -19 through -1 1 through 97 238 -20 through 97 -20 through -1 1 through 97 239 -37 through 14 -37 through -1 1 through 99 240 -27 through 99 -27 through -1 1 through 99 241 -115 through 59 -115 through -1 1 through 99 242 -20 through 32 -20 through -1 1 through 99 243 -20 through 32 -20 th				
213				
214 92 through 177 92 through -1 1 through 177 215 29 -22 through 113 -22 through -1 1 through 173 -21 through 113 -22 through -1 1 through 113 -22 through -1 1 through 113 -22 through -1 1 through 29 -21 through 355 -21 through 355 -21 through -1 1 through 355 -21 through -1 1 through 355 -22 through -1 1 through 181 -30 through -1 1 through 181 -30 through -1 1 through 181 -220 -60 through 94 -60 through -1 1 through 181 -221 -42 through 81 -42 through -1 1 through 81 -222 -19 through 327 -19 through -1 1 through 81 -223 -20 through 190 -20 through -1 1 through 190 -220 through -1 1 through 180 -224 -20 through 164 -20 through -1 1 through 164 -225 -22 through 205 -22 through -1 1 through 164 -225 -22 through 33 -41 through -1 1 through 205 -22 through 73 -1 through 73 -1 through 73 -1 through 73 -1 through 66 -16 through -1 1 through 33 -227 1 through 66 -16 through -1 1 through 66 -229 -56 through 63 -56 through 63 -56 through 63 -1 through 63 -1 through 64 -1 through 65 -1 through 65 -1 through 196 -1 through 197 -1 t				
215 26 -22 through 113 -22 through -1 1 through 113 -216 -38 through 29 -38 through -1 1 through 29 -217 -54 through 71 -54 through -1 1 through 35 -21 through -1 1 through 35 -220 -60 through 94 -60 through -1 1 through 94 -221 -42 through 81 -42 through -1 1 through 81 -222 -19 through 327 -19 through -1 1 through 81 -223 -20 through 180 -20 through -1 1 through 190 -20 through -1 1 through 190 -22 through -1 1 through 64 -225 -22 through -23 -22 through -1 1 through 64 -22 through -1 1 through 65 -22 through -1 1 through 33 -41 through -1 1 through 66 -16 through -1 1 through 67 -17 through 54 -17 through 54 -17 through 54 -17 through 196 -17 through 197 -17 through 297 -17 through 97 -17 throug				
216 -38 through 29 -38 through -1 1 through 29 217 -54 through 71 -54 through 72 -55 through 72 -55 through 73 -55 through 74 -55 through 75 -55 through				
217				
218				
219 -30 through 181 -30 through -1 1 through 181		01 22 04 71		
220 -60 through 94 -60 through -1 1 through 94 -221 -42 through 81 -42 through -1 1 through 327 -19 through 190 -20 through -1 1 through 190 -224 -20 through 164 -20 through -1 1 through 164 -225 -22 through 205 -22 through -1 1 through 205 -22 through -1 1 through 33 -41 through 33 -41 through 33 -41 through 73 1 through 73 -16 through 66 -16 through -1 1 through 66 -229 -56 through 63 -56 through -1 1 through 63 -36 through 54 -3 through 108 -3 through 108 -3 through 108 -3 through 25 -3 through 25 -3 through 294 -3 through 36 -3 through 294 -3 through 36 -3 through 294 -3 through 1 1 through 294 -3 through 1 1 through 297 -3 through 297 -3 through 37 -19 through 97 -3 through 1 1 through 97 -3 through 141 -3 through 37 -3 through 141 -3 through 37 -3 through 141 -3 through 37 -3 through 39 -3 through 141 -3 through 39 -3 through 39 -3 through 39 -3 through 199 -3 through 1 1 through 39 -3 through 39 -3 through 30 -3 through 3				
221 42 through 81 42 through -1 1 through 81 222 -19 through 327 -19 through -1 1 through 327 223 -20 through 190 -20 through -1 1 through 190 224 -20 through 164 -20 through -1 1 through 164 225 -22 through 205 -22 through -1 1 through 205 226 -41 through 33 -4J through -1 1 through 33 227 1 through 66 -16 through -1 1 through 73 228 -16 through 63 -56 through -1 1 through 66 229 -56 through 63 -56 through -1 1 through 63 230 1 through 54 1 through 54 1 through 54 231 -14 through 196 -14 through -1 1 through 196 232 1 through 108 1 through 108 1 through 25 233 -18 through 25 -18 through -1 1 through 26 234 1 through 36 1 through 36 1 through 36 235 -13 through 294 -13 through -1 1 through 294 236 -32 through 74 32 through -1 1 through 37 23				
19 through 327 19 through 1 1 through 327 223 20 through 190 20 through 1 1 through 190 224 20 through 164 20 through 1 1 through 164 225 22 through 205 22 through 1 1 through 205 226 41 through 33 41 through 1 1 through 33 227 1 through 73 1 through 73 1 through 73 1 through 66 229 56 through 66 16 through 1 1 through 63 230 1 through 54 1 through 54 1 through 54 231 14 through 196 14 through 1 1 through 196 232 1 through 108 1 through 108 1 through 108 233 18 through 25 18 through 1 1 through 25 234 1 through 36 13 through 36 13 through 294 13 through 1 1 through 294 236 32 through 74 32 through 1 1 through 274 237 19 through 74 32 through 1 1 through 23 238 20 through 97 20 through 1 1 through 97 239 37 through 141 37 through 1 1 through 141 240 27 through 99 27 through 1 1 through 99 241 115 through 32 39 378 20 through 32 20 through 1 1 through 32 379 23 through 170 23 through 170 1 through 37				
223 20 through 190 20 through 1 1 through 190 224 20 through 164 20 through 1 1 through 164 225 22 through 205 22 through 1 1 through 205 226 41 through 33 43 through 1 1 through 33 227 1 through 66 16 through 1 1 through 73 1 through 66 229 56 through 63 56 through 1 1 through 66 229 56 through 63 56 through 1 1 through 63 230 1 through 54 1 through 54 1 through 196 231 14 through 196 14 through 196 1 through 196 232 1 through 108 1 through 108 1 through 25 234 1 through 25 18 through 1 1 through 25 234 1 through 294 13 through 1 1 through 294 236 32 through 74 32 through 1 1 through 294 237 19 through 23 19 through 1 1 through 23 238 20 through 97 20 through 1 1 through 97 239 37 through 141 37 through 1 1 through 141 240 27 through 99 27 through 1 1 through 59 378 20 through 32 20 through 32 20 through 1 1 through 59 378 20 through 32 20 through 1 1 through 170 23 through 170 24 through 270 through 27				
224 -20 through 164 -20 through -1 1 through 164 225 -22 through 205 -22 through -1 1 through 205 226 -41 through 33 -43 through -1 1 through 33 227 1 through 66 -16 through -1 1 through 66 229 -56 through 63 -56 through -1 1 through 63 230 1 through 54 1 through 54 231 -14 through 196 -14 through -1 1 through 196 232 1 through 108 1 through 108 233 -18 through 25 -18 through -1 1 through 25 234 1 through 36 1 through 36 1 through 36 235 -13 through 294 -13 through -1 1 through 294 236 -32 through 74 32 through -1 1 through 74 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through -1 1 through 97 239 -37 through 141 37 through -1 1 through 99 241 -15 through 59 -15 through -1				
225 -22 through 205 -22 through -1 1 through 205 226 -41 through 33 -43 through -1 1 through 33 227 1 through 73 1 through -1 1 through 73 228 -16 through 66 -16 through -1 1 through 66 229 -56 through 63 -56 through -1 1 through 63 230 1 through 54 1 through -1 1 through 63 231 -14 through 196 -14 through -1 1 through 196 232 1 through 198 1 through 108 1 through 108 233 -18 through 25 18 through -1 1 through 25 234 1 through 36 1 through 36 1 through 36 235 -13 through 294 13 through -1 1 through 294 236 -32 through 74 32 through 1 1 through 74 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through 1 1 through 97 239 -37 through 141 37 through 1 1 through 141 240 -27 thr				
226 -41 through 33 -43 through -1 1 through 33 227 1 through 73 1 through -1 1 through 73 228 -16 through 66 -16 through -1 1 through 66 229 -56 through 63 -56 through -1 1 through 63 230 1 through 54 1 through 54 231 -14 through 196 -14 through -1 1 through 196 232 1 through 108 1 through 108 233 -18 through 25 -18 through -1 1 through 25 234 1 through 36 1 through 25 235 -13 through 294 13 through -1 1 through 294 236 -32 through 74 32 through -1 1 through 74 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through -1 1 through 97 239 -37 through 141 37 through -1 1 through 141 240 -27 through 99 27 through -1 1 through 99 241 -115 through 59 -115 through -1 1 through 99 241 -15 through 32 20 through -1 1 through 170				
227 1 through 73 1 through 73 228 -16 through 66 -16 through -1 1 through 66 229 -56 through 63 -56 through -1 1 through 63 230 1 through 54 1 through 54 231 -14 through 196 -14 through -1 1 through 196 232 1 through 108 1 through 108 233 -18 through 25 -18 through -1 1 through 25 234 1 through 36 1 through 36 235 -13 through 294 13 through -1 1 through 294 236 -32 through 74 32 through -1 1 through 74 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through -1 1 through 97 239 -37 through 141 37 through -1 1 through 141 240 -27 through 99 27 through -1 1 through 99 241 -115 through 59 -115 through -1 1 through 99 241 -115 through 32 20 through -1 1 through 99 241 -115 through 32 20 through -1 1 through 170 <td></td> <td></td> <td></td> <td>1 through 205</td>				1 through 205
228 -16 through 66 -16 through -1 1 through 66 229 -56 through 63 -56 through -1 1 through 63 230 1 through 54 1 through 54 231 -14 through 196 -14 through -1 1 through 196 232 1 through 108 1 through 108 233 -18 through 25 -18 through -1 1 through 25 234 1 through 36 1 through 25 235 -13 through 294 -13 through -1 1 through 294 236 -32 through 74 32 through -1 1 through 74 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through -1 1 through 97 239 -37 through 141 37 through -1 1 through 141 240 -27 through 99 27 through -1 1 through 99 241 -115 through 59 -115 through -1 1 through 59 378 -20 through 32 -20 through -1 1 through 170			-4) through 1	1 through 33
229 -56 through 63 -56 through -1 1 through 63 230 1 through 54 1 through 54 231 -14 through 196 -14 through -1 1 through 196 232 1 through 108 1 through 108 233 -18 through 25 -18 through -1 1 through 25 234 1 through 36 1 through 25 235 -13 through 294 -13 through -1 1 through 294 236 -32 through 74 32 through -1 1 through 74 237 -19 through 23 19 through -1 1 through 23 238 -20 through 97 20 through -1 1 through 97 239 -37 through 141 37 through -1 1 through 141 240 -27 through 99 27 through -1 1 through 99 241 -15 through 59 -15 through -1 1 through 59 378 -20 through 32 -20 through -1 1 through 170			•	1 through 73
1 through 54 1 through 54 1 through 54 231 -14 through 196 -14 through 196 -14 through 196 -14 through 196 -14 through 108 -18 through 108 -18 through 25 -18 through 1 1 through 25 -18 through 25 -13 through 294 -19 through 23 -19 through 23 -19 through 23 -19 through 23 -19 through 97 -19 through 99 -19 through 1 -19 through 199 -19				1 through 66
231			-56 through -1	1 through 63
232 1 through 108 1 through 108 233 -18 through 25 18 through 1 1 through 25 234 1 through 36 1 through 36 1 through 36 235 -13 through 294 -13 through 1 1 through 294 236 -32 through 74 32 through 1 1 through 74 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through 1 1 through 97 239 -37 through 141 37 through 1 1 through 141 240 -27 through 99 27 through 1 1 through 99 241 -15 through 59 -15 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170				1 through 54
233 -18 through 25 -18 through -1 1 through 25 234 1 through 36 1 through 36 235 -13 through 294 -13 through -1 1 through 294 236 -32 through 74 32 through 1 1 through 74 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through 1 1 through 97 239 -37 through 141 37 through -1 1 through 141 240 -27 through 99 27 through 1 1 through 99 241 -115 through 59 -115 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170			-14 through -1	1 through 196
234 1 through 36 1 through 36 235 -13 through 294 -13 through -1 1 through 294 236 -32 through 74 32 through 1 1 through 294 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through 1 1 through 97 239 -37 through 141 37 through -1 1 through 141 240 -27 through 99 27 through 1 1 through 99 241 -115 through 59 -115 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170				1 through 108
235 -13 through 294 -13 through 1 1 through 294 236 -32 through 74 32 through 1 1 through 74 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through 1 1 through 97 239 -37 through 141 37 through 1 1 through 141 240 -27 through 99 27 through 1 1 through 99 241 -115 through 59 -115 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170			-18 through -1	1 through 25
236 -32 through 74 32 through 1 1 through 74 237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through 1 1 through 97 239 -37 through 141 37 through -1 1 through 141 240 -27 through 99 27 through 1 1 through 99 241 -115 through 59 -115 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170				1 through 36
237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through 1 1 through 97 239 -37 through 141 37 through 1 1 through 141 240 -27 through 99 27 through 1 1 through 99 241 -115 through 59 -115 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170			-13 through -1	1 through 294
237 -19 through 23 19 through 1 1 through 23 238 -20 through 97 20 through 1 1 through 97 239 -37 through 141 37 through 1 1 through 141 240 -27 through 99 27 through 1 1 through 99 241 -115 through 59 -115 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170				1 through 74
238 -20 through 97 20 through : 1 through 97 239 -37 through 141 37 through : 1 through 141 240 -27 through 99 27 through 1 1 through 99 241 -115 through 59 -115 through i 1 through 59 378 -20 through 32 -20 through : 1 through 32 379 -23 through 170 -23 through : 1 through 170			19 through 1	1 through 23
239 -37 through 141 37 through 1 1 through 141 240 -27 through 99 27 through 1 1 through 99 241 -115 through 59 -115 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170				
240 -27 through 99 27 through 1 1 through 99 241 -115 through 59 -115 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170			37 through -1	
241 115 through 59 115 through 1 1 through 59 378 -20 through 32 -20 through 1 1 through 32 379 -23 through 170 -23 through 1 1 through 170				
378 20 through 32 20 through 1 1 through 32 379 23 through 170 23 through 1 1 through 170		-115 through 59	-115 through 1	
379 23 through 170 23 through 1 1 through 170			-20 through 1	
		·23 through 170	-23 through 1	
	380	·14 through 68	-14 through 1	1 through 68

\sim	81 T	~		n		•	1
CO.	IV I	. І	Α	o	Ł	Ľ	١

INT. TABLE V			
381	-21 through 177	-21 through -1	1 through 177
382	55 through 105	-55 through -1	1 through 105
383	-18 through 90	-18 through -1	1 through 90
384	-22 through 42	-22 through -1	1 through 42
385	-15 through 12	-15 through -1	1 through 12
386	-21 through 165	-21 through -1	1 through 165
387	-26 through 153	-26 through -1	1 through 153
388	-55 through 95	-55 through -1	1 through 95
389	-31 through 205	-31 through -1	1 through 205
390	-100 through 49	-100 through -1	1 through 49
391	49 through 20	-49 through -1	1 through 20
392	-30 through 211	-30 through -1	1 through 211
393	-30 through 17	-30 through -1	1 through 17
394	-28 through 37	-28 through -1	1 through 37
395	-24 through 49	-24 through -1	1 through 49
396	-18 through 42	-18 through -1	1 through 42
397	-93 through 99	-93 through -1	
398	-72 through 77	72 through 1	1 through 99
399	-20 through 53	-20 through -1	1 through 77
400	-20 through 66	-20 through -1	1 through 53
401	-21 through 57	-20 through -1	1 through 66
402	28 through 37		1 through 57
403	-27 through 184	-28 through -1	1 through 37
404	-80 through 43	-27 through -1	1 through 184
405		-80 through -1	1 through 43
406	-26 through 60 -31 through 131	-26 through -1	1 through 60
407		-31 through -1	1 through 131
408	-37 through 61	37 through 1	1 through 61
409	-15 through 55	-15 through -1	1 through 55
	45 through 15	-45 through -1	1 through 15
410	-22 through 17	-22 through -1	1 through 17
411	-23 through 28	-23 through -1	1 through 28
412	48 through 47	-48 through -1	1 through 47
413	-32 through 28	-32 through -1	1 through 28
414	-79 through 91	-79 through -1	1 through 91
415	-82 through 108	-82 through -1	1 through 108
416	-60 through 54	-60 through -1	1 through 54
417	-108 through 53	-108 through -1	1 through 53
418	-21 through 46	-21 through -1	1 through 46
419	-32 through 300	-32 through -1	1 through 300
420	-19 through 46	-19 through -1	1 through 46
422	-30 through 27	-30 through -1	1 through 27
423	-17 through 68	-17 through -1	1 through 68
424	-17 through 68	-17 through -1	1 through 68
425	-29 through 40	-29 through -1	1 through 40
426	-56 through 66	-56 through -1	1 through 66
427	-30 through 11	-30 through -1	1 through 11
428	-36 through 14	-36 through -1	1 through 14
429	-18 through 118	-18 through -1	1 through 118
430	-65 through 129	65 through -1	1 through 129
431	-69 through 72	-69 through -1	1 through 72
432	-69 through 179	69 through 1	
432 433	-69 through 179 -36 through 13	-69 through -1	1 through 179
432 433 434	-69 through 179 -36 through 13 -14 through 72	-69 through -1 -36 through -1 -14 through -1	1 through 179 1 through 13 1 through 72

CONT. TABLE V

CONT. TABLE V			
436	-16 through 105	-16 through -1	1 through 105
437	-16 through 146	-16 through -1	1 through 146
438	-20 through 90	-20 through -1	1 through 90
439	·15 through 56	-15 through -1	1 through 56
440	-24 through 75	-24 through -1	1 through 75
441	-25 through 144	-25 through -1	1 through 144
442	-76 through 91	-76 through -1	1 through 91
443	15 through 55	-15 through -1	1 through 55
444	-33 through 348	-33 through -1	1 through 348
445	-14 through 25	-14 through -1	1 through 25
446	-37 through 13	-37 through -1	1 through 13
447	-26 through 25	-26 through -1	1 through 25
448	-30 through 212	-30 through -1	1 through 212
449	-60 through 94	-60 through -1	1 through 94
450	-61 through 28	-61 through -1	1 through 28
451	-26 through 47	-26 through -1	1 through 47
452	-34 through 20	-34 through -1	1 through 20
453	-38 through 83	-38 through -1	1 through 83
454	-37 through 129	-37 through -1	1 through 129
455	-26 through 154	-26 through -1	1 through 154
456	-64 through 27	-64 through -1	1 through 27
457	-23 through 234	-23 through -1	1 through 234
458	-60 through 133	-60 through -1	1 through 133
459	28 through 79	-28 through -1	
460	-13 through 108	-13 through -1	1 through 79
461	-17 through 27	-17 through -1	1 through 108
462	-17 through 96		1 through 27
463	-41 through 102	-13 through -1 -41 through -1	1 through 96
464	-30 through 202	-30 through -1	1 through 102
465	-21 through 40	-21 through -1	1 through 202
466	-19 through 15	-19 through -1	1 through 40 1 through 15
467	-54 through 161	-54 through -1	
468	-17 through 10		1 through 161
469	-24 through 61	-17 through -1	1 through 10
470	-16 through 35	-24 through -1	1 through 61
471	-43 through 24	-16 through -1	1 through 35
472		-43 through -1	1 through 24
473	-15 through 48	-15 through -1	1 through 48
474	58 through 121	-58 through -1	1 through 121
475	-71 through 167 -37 through 141	-71 through -1	1 through 167
476		-37 through -1	1 through 141
477	-21 through 75	-21 through -1	1 through 75
	-24 through 17	-24 through -1	1 through 17
478	-27 through 86	-27 through -1	1 through 86
479	-18 through 232	-18 through -1	1 through 232
480	-21 through 130	-21 through -1	1 through 130
481	25 through 214	25 through 1	1 through 214
482	92 through 116	92 through ·1	1 through 116
483	39 through 47	-39 through -1	1 through 47
484	27 through 13	-27 through -1	1 through 13
485	-16 through 49	-16 through -1	1 through 49
486	-55 through 75	-55 through -1	1 through 75
487	-84 through 125	-84 through -1	1 through 125
488	-17'through 19	-17 through -1	1 through 19
489	29 through 15	-29 through -1	1 through 15

490	-52 through 111	-52 through -1	1 through 111
491	-47 through 17	-47 through -1	1 through 17
492	50 through 168	-50 through -1	1 through 168
493	-15 through 201	-15 through -1	1 through 201
494	-19 through 115	-19 through -1	1 through 115
495	-16 through 69	-16 through -1	1 through 69
496	-29 through 263	-29 through -1	1 through 263
497	-56 through 66	-56 through -1	1 through 66
498	-28 through 31	-28 through -1	1 through 31
499	-13 through 86	-13 through -1	1 through 86
500	-13 through 86	·13 through ·1	1 through 86
501	-25 through 83	-25 through -1	1 through 83
502	-15 through 168	-15 through -1	1 through 168
503	-15 through 83	-15 through -1	1 through 83
504	57 through 126	-57 through -1	1 through 126
505	-14 through 126	-14 through -1	1 through 126
506	-14 through 45	-14 through -1	1 through 45
507	-36 through 65	-36 through -1	1 through 65
508	-55 through 286	-55 through -1	1 through 286
509	42 through 66	-42 through -1	1 through 66
510	-26 through 54	-26 through -1	1 through 54
511	-44 through 114	-44 through -1	1 through 114
512	-28 through 102	-28 through -1	1 through 102
513	-62 through 137	-62 through -1	1 through 137
514	25 through 155	-25 through -1	1 through 155

-120-

TABLE VI

14	Callagain	
ld	Collection refs	Deposit Name
40	ATCC # 98921	SignalTag 121-144
41	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
42	ATCC # 98921	SignalTag 121-144
43	ATCC # 98920	SignalTag 67-90
44	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
45	ATCC # 98920	SignalTag 67-90
46	ATCC # 98923	SignalTag 44-66
47	ATCC # 98920	SignalTag 67-90
48	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
49	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
50	ATCC # 98921	SignalTag 121-144
51	ATCC # 98921	SignalTag 121-144
52	ATCC # 98920	SignalTag 67-90
53	ATCC # 98923	SignalTag 44-66
54	ATCC # 98920	SignalTag 67-90
55	ATCC # 98920	SignalTag 67-90
56	ATCC # 98920	SignalTag 67-90
57	ATCC # 98921	SignalTag 121-144
58	ATCC # 98920	SignalTag 67-90
59	ATCC # 98920	SignalTag 67-90
60	ATCC # 98920	SignalTag 67-90
61	ATCC # 98923	SignalTag 44-66
62	ATCC # 98923	SignalTag 44-66
63	ATCC # 98923	SignalTag 44-66
64	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
65	ATCC # 98923	SignalTag 44-66
66	ATCC # 98921	SignalTag 121-144
67	ATCC # 98920	SignalTag 67-90
68	ATCC # 98920	SignatTag 67-90
69	ATCC # 98921	SignalTag 121-144
70	ATCC # 98921	SignalTag 121-144
71	ATCC # 98921	Signal Tag 121-144
72	ATCC # 98922	SignalTag 91 94, 96, 97, 99 107, 109 112 et 114 120
73	ATCC # 98923	SignalTag 44-66

74	ATCC # 98923	SignalTag 44-66
75	ATCC # 98920	SignalTag 67-90
76	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
77	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
78	ATCC # 98921	SignalTag 121-144
79	ATCC # 98923	SignalTag 44-66
80	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
81	ATCC # 98921	SignalTag 121-144
82	ATCC # 98920	SignalTag 67-90
83	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
84	ATCC # 98923	SignalTag 44-66
85	ATCC # 98923	SignalTag 44-66
86	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
87	ATCC # 98923	SignalTag 44-66
88	ATCC # 98923	SignalTag 44-66
89	ATCC # 98923	SignalTag 44-66
90	ATCC # 98923	SignalTag 44-66
91	ATCC # 98923	SignalTag 44-66
92	ATCC # 98920	SignalTag 67-90
93	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
94	ATCC # 98923	SignalTag 44-66
95	ATCC # 98923	SignalTag 44-66
96	ATCC # 98920	SignalTag 67-90
97	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
98	ATCC # 98921	SignalTag 121-144
99	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
100	ATCC # 98921	SignalTag 121-144
101	ATCC # 98920	SignalTag 67-90
102	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
103	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
104	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
105	ATCC # 98921	SignalTag 121-144
106	ATCC # 98920	SignalTag 67-90
107	ATCC # 98920	SignalTag 67-90
108	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
109	ATCC # 98923 ,	SignalTag 44-66
110	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120

111	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120.
112	ATCC # 98920	SignalTag 67-90
113	ATCC # 98920	SignalTag 67-90
114	ATCC # 98923	SignalTag 44-66
115	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
116	ATCC # 98920	SignalTag 67-90
117	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
118	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
119	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
120	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
121	ATCC # 98923	SignalTag 44-66
122	ATCC # 98920	SignalTag 67-90
123	ATCC # 98920	SignalTag 67-90
124	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
125	ECACC # 98121506	SignalTag 11121998
126	ECACC # 98121506	SignalTag 11121998
127	ECACC # 98121506	SignalTag 11121998
128	ECACC # 98121506	SignalTag 11121998
129	ECACC # 98121506	SignalTag 11121998
130	ECACC # 98121506	SignalTag 11121998
131	ECACC # 98121506	SignalTag 11121998
132	ECACC # 98121506	SignalTag 11121998
133	ECACC # 98121506	SignalTag 11121998
134	ECACC # 98121506	SignalTag 11121998
135	ECACC # 98121506	SignalTag 11121998
136	ECACC # 98121506	SignalTag 11121998
137	ECACC # 98121506	SignalTag 11121998
138	ECACC # 98121506	SignalTag 11121998
139	ECACC # 98121506	SignalTag 11121998
140	ECACC # 98121506	SignalTag 11121998
		_ I.

-123-TABLE VII

Internal designation number	SEQ ID NO	Type of sequence	
20-5-2-C3-CL0_4	40	DNA	
20-8-4-A11-CL2_6	41	DNA	
21-1-4-F2-CL11_1	42	DNA	
22-11-2-H9-CL1_1	43	DNA	
25-7-3-D4-CL0_2	44	DNA	
26-27-3-07-CLO_1	45	DNA	
26-35-4-H9-CL1_1	46	DNA	
26-45-2-C4-CL2_6	47	DNA	
27-1-2-B3-CL0_1	48	DNA	
27-1-2-B3-CL0_2	49	DNA	
27-19-3-G7-CL11_2	50	DNA	
33-10-4-E2-CL13_4	51	DNA	
33-10-4-H2-CL2_2	52	DNA	
33-110-4-A5-CL1_1	53	DNA	
33-13-1-C1-CL1_1	54	DNA	
33-30-2-A6-CLO_1	55	DNA	
33-35-4-F4-CL1_2	56	DNA	
33-35-4-G1-CL1_2	57	DNA	
33-36-3-E2-CL1_1	58	DNA	
33-36-3-E2-CL1_2	59	DNA	
33-36-3-F2-CL2_2	60	DNA	
33-4-2-G5-CL2_1	61	DNA	
33-49-1-H4-CL1_1	62	DNA	
33-66-2-B10-CL4_1	63	DNA	
33-97-4-G8-CL2_2	64	DNA	
33-98-4-C1-CL1_3	65	DNA	
47-14-1-C3-CL0_5	66	DNA	
47-15-1-E11-CLO_1	67	DNA	
47-15-1-H8-CLO_2	68	DNA	
48-1-1-H7-CLO_1	69	DNA	
48-1-1-H7-CLO_4	70	DNA	
48-1-1-H7-CLO_5	71	CNA	
48-3-1-H9-CLO_6	72	ONA	
48-54-1-G9-CL2_1	73	DNA	

48-54-1-69-CL3_1	74	DNA
48-7-4-H2-CL2_2	75	DNA
51-11-3-05-CL1_3	76	DNA
51-11-3-G9-CLO_1	77	DNA
51-15-4-A12-CL11_3	78	DNA
51-17-4-A4-CL3_1	79	DNA
51-2-3-F10-CL1_5	80	DNA
51-2-4-F5-CL11_2	81	DNA
51-27-4-F2-CLO_2	82	DNA
51-34-3-F8-CLO_2	83	DNA
57-1-4-E2-CL1_2	84	DNA
57-19-2-G8-CL2_1	85	DNA
57-27-3-G10-CL2_2	86	DNA
58-33-3-B4-CL1_2	87	DNA
58-34-3-C9-CL1_2	88	DNA
58-4-4-G2-CL2_1	89	DNA
58-48-1-G3-CL2_4	90	DNA
58-6-1-H4-CL1_1	91	DNA
60-12-1-E11-CL1_2	92	DNA
65-4-4-H3-CL1_1	93	DNA
74-5-1-E4-CL1_2	94	DNA
76-13-3-A9-CL1_2	95	DNA
76-16-1-D6-CL1_1	96	DNA
76-28-3-A12-CL1_5	97	DNA
76-42-2-F3-CLO_1	98	ONA
77-16-4-G3-CL1_3	99	DNA
77-39-4-H4-CL11_4	100	DNA
78-24-3-H4-CL2_1	101	DNA
78-27-3-D1-CL1_6	102	DNA
78-28-3-D2-CLO_2	103	DNA
78-7-1-G5-CL2_6	104	DNA
84-3-1-G10-CL11_6	105	DNA
58-48-4-E2-CLO_1	106	DNA
23-12-2-G6-CL1_2	107	DNA
25-8-4-B12-CLO_5	108	DNA
26-44-3-C5-CL2_1	109	DNA
27-1-2-83-CLO_3	110	DNA

		.5
30-12-3-G5-CLO_1	111	DNA
33-106-2-F10-CL1_3	112	DNA
33-28-4-D1-CLO_1	113	DNA
33-31-3-C8-CL2_1	114	DNA
48-24-1-D2-CL3_2	115	DNA
48-46-4-A11-CL1_4	116	DNA
51-1-4-C1-CLO_2	117	DNA
51 39 3 H2 CL1_2	118	DNA
51-42-3-F9-CL1_1	119	DNA
51-5-3-G2-CLO_4	120	DNA
57-18-4-H5-CL2_1	121	DNA
76-23-3-G8-CL1_1	122	DNA
76-23-3-G8-CL1_3	123	DNA
78-8-3-E6-CLO_1	124	DNA
19-10-1-C2-CL1_3	125	DNA
33-11-1-B11-CL1_2	126	DNA
33-113-2-B8-CL1_2	127	ONA
33-19-1-C11-CL1_1	128	DNA
33-61-2-F6-CLO_2	129	DNA
47-4-4-C6-CL2_2	130	DNA
48-54-1-G9-CL1_1	131	DNA
51-43-3-G3-CLO_1	132	DNA
55-1-3-D11-CLO_1	133	DNA
58-14-2-D3-CL1_2	134	DNA
58-35-2-86-CL2_3	135	DNA
76-18-1-F6-CL1_1	136	DNA
76-23-3-G8-CL2_2	137	DNA
76-30-3-B7-CL1_1	138	DNA
78-21-3-G7-CL2_1	139	DNA
58-45-4-B11-CL13_2	140	DNA
20-5-2-C3-CL0_4	141	PRT
20-8-4-A11-CL2_6	142	PRT
21-1-4-F2-CL11_1	143	PRT
22-11-2-H9-CL1_1	144	PRT
25-7-3-D4-CLO_2	145	PRT
26-27-3-07-CL0_,1	146	PRT
26-35-4-H9-CL1_1	147	PRT

26-45-2-C4-CL2_6	148	PRT
27-1-2-B3-CLO_1	149	PRT
27-1-2-B3-CLO_2	150	PRT
27-19-3-G7-CL11_2	151	PRT
33-10-4-E2-CL13_4	152	PRT
33-10-4-H2-CL2_2	153	PRT
33-110-4-A5-CL1_1	154	PRT
33-13-1-C1-CL1_1	155	PRT
33-30-2-A6-CLO_1	156	PRT
33-35-4-F4-CL1_2	157	PRT
33-35-4-G1-CL1_2	158	PRT
33-36-3-E2-CL1_1	159	PRT
33-36-3-E2-CL1_2	160	PRT
33-36-3-F2-CL2_2	161	PRT
33-4-2-G5-CL2_1	· 162	PRT
33-49-1-H4-CL1_1	163	PRT
33-66-2-B10-CL4_1	164	PRT
33-97-4-G8-CL2_2	165	PRT
33-98-4-C1-CL1_3	166	PRT
47-14-1-C3-CL0_5	167	PRT
47-15-1-E11-CL0_1	168	PRT
47-15-1-H8-CLO_2	169	PRT
48-1-1-H7-CLO_1	170	PRT
48-1-1-H7-CLO_4	171	PRT
48-1-1-H7-CLO_5	172	PRT
48-3-1-H9-CLO_6	173	PRT
48-54-1-G9-CL2_1	174	PRT
48-54-1-G9-CL3_1	175	PRT
48-7-4-H2-CL2_2	176	PRT
51-11-3-D5-CL1_3	177	PRT
51-11-3-G9-CLO_1	178	PRT
51-15-4-A12-CL11_3	179	PRT
51-17-4-A4-CL3_1	180	PRT
51-2-3-F10-CL1_5	181	PRT
51-2-4-F5-CL11_2	182	PRT
51-27-4-F2-CL0_2	183	PRT
51-34-3-F8-CLO_2	184	PRT
51-34-3-F8-CLO_2	184	PRI

57-1-4-E2-CL1_2	185	PRT
57-19-2-G8-CL2_1	186	PRT
57-27-3-G10-CL2_2	187	PRT
58-33-3-84-CL1_2	188	PRT
58-34-3-C9-CL1_2	189	PRT
58-4-4-G2-CL2_1	190	PRT
58-48-1-G3-CL2_4	191	PRT
58-6-1-H4-CL1_1	192	PRT
60-12-1-E11-CL1_2	193	PRT
65-4-4-H3-CL1_1	194	PRT
74-5-1-E4-CL1_2	195	PRT
76-13-3-A9-CL1_2	196	PRT
76-16-1-D6-CL1_1	197	PRT
76-28-3-A12-CL1_5	198	PRT
76-42-2-F3-CLO_1	199	PRT
77-16-4-G3-CL1_3	200	PRT
77-39-4-H4-CL11_4	201	PRT
78-24-3-H4-CL2_1	202	PRT
78-27-3-D1-CL1_6	203	PRT
78-28-3-D2-CLO_2	204	PRT
78-7-1-G5-CL2_6	205	PRT
84-3-1-G10-CL11_6	206	PRT
58-48-4-E2-CLO_1	207	PRT
23-12-2-G6-CL1_2	208	PRT
25-8-4-B12-CL0_5	209	PRT
26-44-3-C5-CL2_1	210	PRT
27-1-2-B3-CL0_3	211	PRT
30-12-3- G5-CLO_1	212	PRT
33-106-2-F10-CL1_3	213	PRT
33-28-4-D1-CLO_1	214	PRT
33-31-3-C8-CL2_1	215	PRT
48-24-1-D2-CL3_2	216	PRT
48-46-4-A11-CL1_4	217	PRT
51-1-4-C1-CL0_2	218	PRT
51-39-3-H2-CL1_2	219	PRT
51-42-3-F9-CL1_1	220	PRT
51-5-3-G2-CLO_4	221	PRT
<u> </u>		

57-18-4-H5-CL2_1	222	PRT
76-23-3-G8-CL1_1	223	PRT
76-23-3-G8-CL1_3	224	PRT
78-8-3-E6-CLO_1	225	PRT
19-10-1-C2-CL1_3	226	PRT
33-11-1-B11-CL1_2	227	PRT
33-113-2-B8-CL1_2	228	PRT
33-19-1-C11-CL1_1	229	PRT
33-61-2-F6-CLO_2	230	PRT
47-4-4-C6-CL2_2	231	PRT
48-54-1-G9-CL1_1	232	- PRT
51-43-3-G3-CLO_1	233	PRT
55-1-3-D11-CLO_1	234	PRT
58-14-2-D3-CL1_2	235	PRT
58-35-2-B6-CL2_3	236	PRT
76-18-1-F6-CL1_1	237	PRT
76-23-3-G8-CL2_2	238	PRT
76-30-3-B7-CL1_1	239	PRT
78-21-3-G7-CL2_1	240	PRT
58-45-4-B11-CL13_2	241	PRT
20-6-1-D11-FL2	242	DNA
20-8-4-A11-FL2	243	DNA
22-6-2-C1-FL2	244	DNA
22-11-2-H9-FL1	245	DNA
23-8-3-B1-FL1	246	DNA
24-3-3-C6-FL1	247	ONA
24-4-1-H3-FL1	248	DNA
26-45-2-C4-FL2	249	DNA
26-48-1-H10-FL1	250	DNA
26-49-1-A5-FL2	251	DNA
30-6-4-E3-FL3	252	ONA
33-6-1-G11-FL1	253	DNA
33-8-1-A3-FL2	254	DNA
33-11-3-C6-FL1	255	DNA
33-14-4-E1-FL1	256	ONA
33-21-2-D5-FL1	257	DNA
33-26-4-E10-FL1	258	DNA

33-27-1-E11-FL1	259	DNA
33-28-4-D1-FL1	260	DNA
33-28-4-E2-FL2	261	DNA
33-30-4-C4-FL1	262	DNA
33-35-4-F4-FL1	263	DNA
33-36-3-F2-FL2	264	DNA
33-52-4-F9-FL2	265	DNA
33-52-4-H3-FL1	266	DNA
33-59-1-B7-FL1	267	DNA
33-71-1-A8-FL1	268	DNA
33-72-2-82-FL1	269	DNA
33-105-2-C3-FL1	270	DNA
33-107-4-C3-FL1	271	DNA
33-110-2-G4-FL1	272	DNA
47-7-4-02-FL2	273	DNA
47-10-2-G12-FL1	274	DNA
47-14-3-08-FL1	275	DNA
47-18-3-C2-FL1	276	DNA
47-18-3-G5-FL2	277	DNA
47-18-4-E3-FL2	278	DNA
48-3-1-H9-FL3	279	DNA
48-4-2-H3-FL1	280	DNA
48-6-1-C9-FL1	281	DNA
48-7-4-H2-FL2	282	DNA
48-8-1-D8-FL3	283	DNA
48-13-3-H8-FL1	284	DNA
48-19-3-A7-FL1	285	DNA
48-19-3-G1-FL1	286	DNA
48-25-4-D8-FL1	287	DNA
48-21-4-H4-FL1	288	DNA
48-26-3-B8-FL2	289	DNA
48-29-1-E2-FL1	290	DNA
48-31-3-F7-FL1	291	DNA
48-47-3-A5-FL1	292	DNA
51-1-1-G12-FL1	293	DNA
51-1-4-E9-FL3	294	DNA
51-1-4-E9-FL2	295	DNA

51-2-1-E10-FL1	296	DNA
51-2-3-F10-FL1	297	DNA
51-2-4-F5-FL1	298	DNA
51-3-3-810-FL2	299	DNA
51-3-3-B10-FL3	300	DNA
51-7-3-G3-FL1	301	DNA
51-10-3-D11-FL1	302	DNA
51-11-3-D5-FL1	303	DNA
51-13-1-F7-FL3	304	DNA
51-15-4-H10-FL1	305	DNA
51-17-4-A4-FL1	306	ONA
51-18-1-C3-FL1	307	DNA
51-25-3-F3-FL1	308	DNA
51-27-1-E8-FL1	309	DNA
51-28-2-G1-FL2	310	DNA
51-39-3-H2-FL1	311	DNA
51-42-3-F9-FL1	312	DNA
51-44-4-H4-FL1	313	DNA
55-1-3-H10-FL1	314	DNA
55-5-4-A6-FL1	315	DNA
58-26-3-D1-FL1	316	DNA
57-18-1-D5-FL1	317	DNA
57-27-3-A11-FL1	318	DNA
57-27-3-G10-FL2	319	DNA
58-10-3-012-FL1	320	DNA
58-11-1-G10-FL1	321	DNA
58-11-2-G8-FL2	322	DNA
58-36-3-A9-FL2	323	DNA
58-38-1-A2-FL2	324	DNA
58-38-1-E5-FL1	325	DNA
58-44-2-B3-FL3	326	DNA
58-45-3-H11-FL1	327	DNA
58-53-2-B12-FL2	328	DNA
59-9-4-A10-FL1	329	DNA
60-16-3-A6-FL1	330	DNA
60-17-3-G8-FL2	331	DNA
62-5-4-B10-FL1	332	DNA

65-4-4-H3-FL1	333	DNA
74-3-1-89-FL1	334	DNA
76-4-1-G5-FL1	335	DNA
76-7-3-A12-FL1	336	DNA
76-16-4-C9-FL3	337	DNA
76-30-3-87-FL1	338	DNA
77-5-1-C2-FL1	339	ONA
77-5-4-E7-FL1	340	DNA
77-11-1-A3-FL1	341	DNA
77-16-3-D7-FL1	342	DNA
77-16-4-G3-FL1	343	DNA
77-25-1-A6-FL1	344	DNA
77-26-2-F2-FL3	345	DNA
78-6-2-E3-FL2	346	DNA
78-7-1-G5-FL2	347	DNA
78-16-2-C2-FL1	348	DNA
78-18-3-84-FL3	349	DNA
78-20-1-G11-FL1	350	DNA
78-22-3-E10-FL1	351	DNA
78-24-2-88-FL1	352	DNA
78-24-3-A8-FL1	353	DNA
78-24-3-H4-FL2	354	DNA
78-25-1-F11-FL1	355	DNA
78-26-1-B5-FL1	356	DNA
78-27-3-01-FL1	357	- DNA
78-29-1-B2-FL1	358	DNA
78-29-4-B6-FL1	359	DNA
14-1-3-E6-FL1	360	DNA
30-9-1-G8-FL2	361	ONA
33-10-4-H2-FL2	362	DNA
33-10-4-H2-FL1	363	DNA
74-10-3-C9-FL2	364	DNA
33-97-4-G8-FL3	365	DNA
33-97-4-G8-FL2	366	DNA
33-104-4-H4-FL1	367	DNA
47-2-3-B3-FL1	368	DNA
47-37-4-G11-FL1	369	DNA
		

57-25-1-F10-FL2	370	DNA
58-19-3-03-FL1	371	DNA
58-34-3-C9-FL2	372	DNA
58-48-4-E2-FL2	373	DNA
76-21-1-C4-FL1	374	DNA
78·26-2·H7-FL1	375	DNA
77-20-2-E11-FL1	376	DNA
47-1-3-F7-FL2	377	DNA
20-6-1-011-FL2	378	PRT
20-8-4-A11-FL2	379	PRT
22-6-2-C1-FL2	380	PRT
22-11-2-H9-FL1	381	PRT
23-8-3-B1-FL1	382	PRT
24-3-3-C6-FL1	383	PRT
24-4-1-H3-FL1	384	PRT
26-45-2-C4-FL2	385	PRT
26-48-1-H10-FL1	386	PRT
26-49-1-A5-FL2	387	PRT
30-6-4-E3-FL3	388	PRT
33-6-1-G11-FL1	389	PRT
33-8-1-A3-FL2	390	PRT
33-11-3-C6-FL1	391	PRT
33-14-4-E1-FL1	392	PRT
33-21-2-D5-FL1	393	PRT
33-26-4-E10-FL1	394	PRT
33-27-1-E11-FL1	395	PRT
33-28-4-D1-FL1	396	PRT
33-28-4-E2-FL2	397	PRT
33-30-4-C4-FL1	398	PRT
33-35-4-F4-FL1	399	PRT
33-36-3-F2-FL2	400	PRT
33-52-4-F9-FL2	401	PRT
33-52-4-H3-FL1	402	PRT
33-59-1-B7-FL1	403	PRT
33-71-1-A8-FL1	404	PRT
33-72-2-B2-FL1	405	PRT
33 105-2-C3-FL1	406	PRT

33-107-4-C3-FL1	407	PRT
33-110-2-G4-FL1	408	PRT
47-7-4-D2-FL2	409	PRT
47-10-2-G12-FL1	410	PRT
47-14-3-08-FL1	411	PRT
47-18-3-C2-FL1	412	PRT
47-18-3-G5-FL2	413	PRT
47-18-4-E3-FL2	414	PRT
48-3-1-H9-FL3	415	PRT
48-4-2-H3-FL1	416	PRT
48-6-1-C9-FL1	417	PRT
48-7-4-H2-FL2	418	PRT
48-8-1-D8-FL3	419	PRT
48-13-3-H8-FL1	420	PRT
48-19-3-A7-FL1	421	PRT
48-19-3-G1-FL1	422	PRT
48-25-4-D8-FL1	423	PRT
48-21-4-H4-FL1	424	PRT
48-26-3-88-FL2	425	PRT
48-29-1-E2-FL1	426	PRT
48-31-3-F7-FL1	427	PRT
48-47-3-A5-FL1	428	PRT
51-1-1-G12-FL1	429	PRT
51-1-4-E9-FL3	430	PRT
51-1-4-E9-FL2	431	PRT
51-2-1-E10-FL1	432	PRT
51-2-3-F10-FL1	433	PRT
51-2-4-F 5 -FL1	434	PRT
51-3-3-B10-FL2	435	PRT
51-3-3-B10-FL3	436	PRT
51-7-3-G3-FL1	437	PRT
51-10-3-D11-FL1	438	PRT
51-11-3- D5-FL1	439	PRT
51-13-1-F7-FL3	440	PRT
51-15-4-H10-FL1	441	PRT
51-17-4-A4-FL1	442	PRT
51-18-1-C3-FL1	443	PFT
	_ <u></u>	

·	-10) - -
51-25-3-F3-FL1	444	PRT
51-27-1-E8-FL1	445	PRT
51-28-2-G1-FL2	446	PRT
51-39-3-H2-FL1	447	PRT
51-42-3-F9-FL1	448	PRT
51-44-4-H4-FL1	449	PRT
55-1-3-H10-FL1	450	PRT
55-5-4-A6-FL1	451	PRT
58-26-3-D1-FL1	452	PRT
57-18-1-05-FL1	453	PRT
57-27-3-A11-FL1	454	PRT
57-27-3-G10-FL2	455	PRT
58-10-3-D12-FL1	456	PRT
58-11-1-G10-FL1	457	PRT
58-11-2-G8-FL2-	458	PRT
58-36-3-A9-FL2	459	PRT
58-38-1-A2-FL2	460	PRT
58-38-1-E5-FL1	461	PRT
58-44-2-83-FL3	462	PRT
58-45-3-H11-FL1	463	PRT
58-53-2-B12-FL2	464	PRT
59-9-4-A10-FL1	465	PRT
60-16-3-A6-FL1	466	PRT
60-17-3-G8-FL2	467	PRT
62-5-4-B10-FL1	468	PRT
65-4-4-H3-FL1	469	PRT
74-3-1-B9-FL1	470	PRT
76-4-1-G5-FL1	471	PRT
76-7-3-A12-FL1	472	PRT
76-16-4-C9-FL3	473	PRT
76-30-3-87-FL1	474	PRT
77-5-1-C2-FL1	475	PRT
77-5-4-E7-FL1	476	PRT
77-11-1-A3-FL1	477	PRT
77-16-3-D7-FL1	478	PRT
77-16-4-G3-FL1	479	PRT
77-25-1-A6-FL1	480	PRT

77-26-2-F2-FL3	481	PRT
78-6-2-E3-FL2	482	PRT
78-7-1-G5-FL2	483	PRT
78-16-2-C2-FL1	484	PRT
78-18-3-B4-FL3	485	PRT
78-20-1-G11-FL1	486	PRT
78-22-3-E10-FL1	487	PRT
78-24-2-88-FL1	488	PRT
78-24-3-A8-FL1	489	PRT
78-24-3-H4-FL2	490	PRT
78-25-1-F11-FL1	491	PRT
78-26-1-85-FL1	492	PRT
78-27-3-D1-FL1	493	PRT
78-29-1-B2-FL1	494	PRT
78-29-4-86-FL1	495	PRT
14-1-3-E6-FL1	496	PRT
30-9-1-G8-FL2	497	PRT
33-10-4-H2-FL2	498	PRT
33-10-4-H2-FL1	499	PRT
74-10-3-C9-FL2	500	PRT
33-97-4-G8-FL3	501	PRT
33-97-4-G8-FL2	502	PRT
33-104-4-H4-FL1	503	PRT
47-2-3-B3-FL1	504	PRT
47-37-4-G11-FL1	505	PRT
57-25-1-F10-FL2	506	PRT
58-19-3-D3-FL1	507	PRT
58-34-3-C9-FL2	508	PRT
58-48-4-E2-FL2	509	PRT
76-21-1-C4-FL1	510	PRT
78-26-2-H7-FL1	511	PRT
77-20-2-E11-FL1	512	PRT
47-1-3-F7-FL2	513	PRT

-136-

TABLE VIII

ID.	Locations	PROSITE Signature Name
195	110-121	Aldehyde dehydrogenases csyteine active site
221	28-37	ATP synthase alpha and beta subunits signature
223	171-181	Regulator of chromosome condensation (RCC1) signature 2
225	90-112	Phosphatidylethanolamine-binding protein family signature
226	10-34	Protein kinases ATP-binding region signature

WHAT IS CLAIMED IS:

- 1. A purified or isolated nucleic acid comprising the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary thereto.
- 2. A purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 40-140 and 242-377 or one of the sequences complementary thereto.
 - 3. A purified or isolated nucleic acid comprising the full coding sequences of one of SEQ ID NOs: 40, 42-44, 46, 48, 49, 51, 53, 60, 62-72, 76-78, 80-83, 85-88, 90, 93, 94, 97, 99-102, 104, 107-125, 127, 132, 135-138, 140 and 242-377 wherein the full coding sequence comprises the sequence encoding signal peptide and the sequence encoding mature protein.
- A purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40-44, 46, 48,
 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode a mature protein.
- 5. A purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40, 42-46, 48, 49, 51, 53, 57, 60, 62-73, 76-78, 80-83, 85-88, 90, 93-95, 97, 99-102, 104, 107-125, 127, 128, 130, 132, 134-140 and 242-377 which encode the signal peptide.
 - 6. A purified or isolated nucleic acid encoding a polypeptide having the sequence of one of the sequences of SEQ ID NOs: 141-241 and 378-513.
- A purified or isolated nucleic acid encoding a polypeptide having the sequence of a mature protein included in one of the sequences of SEO ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-20
 189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.
 - 8. A purified or isolated nucleic acid encoding a polypeptide having the sequence of a signal peptide included in one of the sequences of SEO ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.
 - A purified or isolated protein comprising the sequence of one of SEQ ID NOs: 141-241 and 378-513.
- 25 10. A purified or isolated polypeptide comprising at least 10 consecutive amino acids of one of the sequences of SEO ID NOs: 141-241 and 378-513.
 - An isolated or purified polypeptide comprising a signal peptide of one of the polypeptides of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.
- 30 12. An isolated or purified polypeptide comprising a mature protein of one of the polypeptides of SEQ ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.
 - 13. A method of making a protein comprising one of the sequences of SEQ ID NO: 141-241 and 378-513, comprising the steps of:

obtaining a cDNA comprising one of the sequences of sequence of SEQ ID NO: 40-140 and 242-377; inserting said cDNA in an expression vector such that said cDNA is operably linked to a promoter; and introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA.

- 5 14. The method of Claim 13, further comprising the step of isolating said protein.
 - 15. A protein obtainable by the method of Claim 14.
 - 16. A host cell containing a recombinant nucleic acid of Claim 1.
 - 17. A purified or isolated antibody capable of specifically binding to a protein having the sequence of one of SEQ ID NOs: 141-241 and 378-513.
- 10 18. In an array of polynucleotides of at least 15 nucleotides in length, the improvement comprising inclusion in said array of at least one of the sequences of SEQ ID NOs: 40-140 and 242-377, or one of the sequences complementary to the sequences of SEQ ID NOs: 40-140 and 242-377, or a fragment thereof of at least 15 consecutive nucleotides.
- 19. A purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent
 15 conditions to the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary to one of the sequences of SEQ ID NOs: 40-140 and 242-377.
 - A purified or isolated antibody capable of binding to a polypeptide comprising at least 10 consecutive amino acids of the sequence of one of SEQ ID NOs: 141-241 and 378-513.

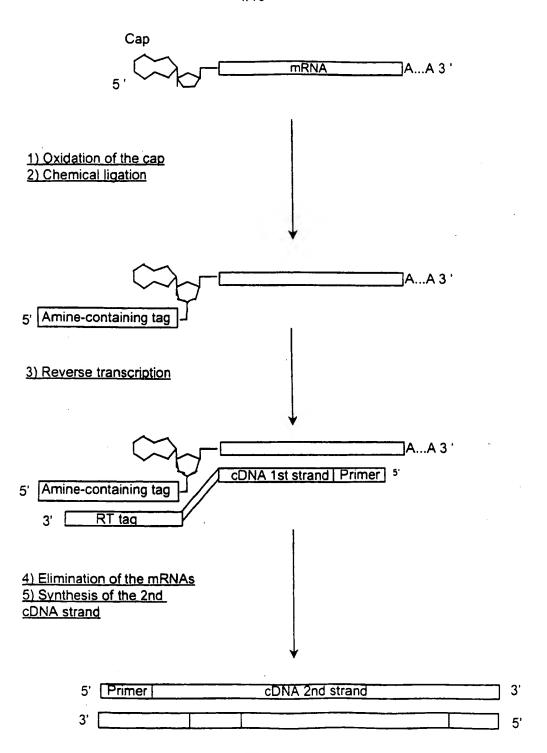


Figure 1

Minimum signal peptide score	false positive rate	false negative rate	proba(0.1)	proba(0.2)
3,5	0,121	0,036	0,467	0,664
4	0,096	0,06	0,519	0,708
4,5	0,078	0,079	0,565	0,745
5	0,062	0,098	0,615	0,782
5,5	0,05	0,127	- 0,659	0,813
6	ાકો 0,04	0,163	0,694	0,836
6,5	301 0,033	0,202	0,725	0,855
7	^{Ot,} 0,025	0,248	0,763	0,878
7,5	0,021	0,304	0,78	0,889
8	0,015	0,368	0,816	0,909
8,5	0,012	0,418	0,836	0,92
9	0,009	0,512	0,856	0,93
9,5	0,007	0,581	0,863	0,934
10	0,006	0,679	0,835	0,919

influence of minimum score on signal peptide recognition

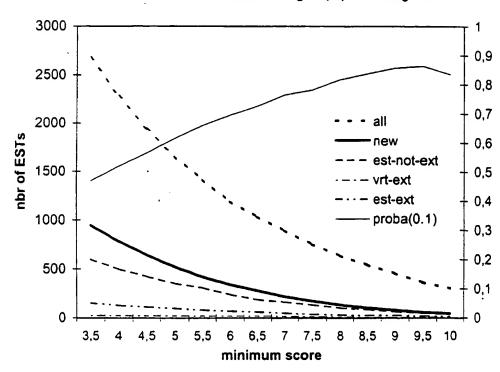
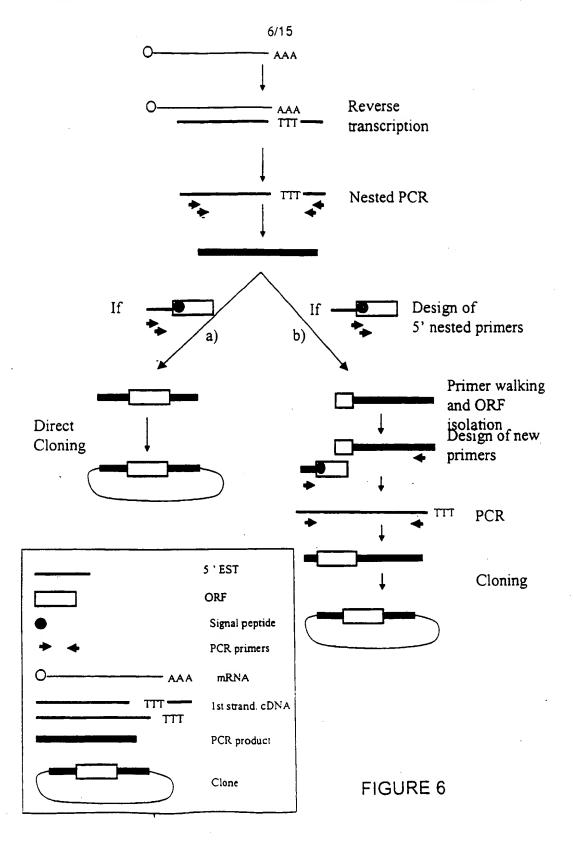


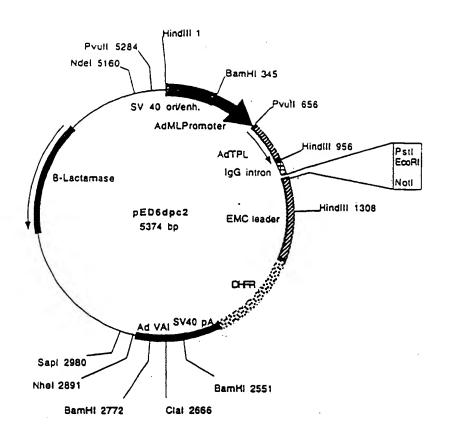
FIGURE 3

Minimum signal peptide score	-	New ESTs	40 bp from beginning	ESTs extending known mRNA more than 40 bp	ESTs extending public EST more than 40 bp
3,5	2674	947	599	23	150
4	2278	784	499	23	126
4,5	1943	647	425	22	112
5	1657	523	353	21	96
5,5	1417	419	307	19	80
6	1190	340	238	18	68
6,5	1035	280	186	18	60
7	893	219	161	15	48
7,5	753	173	132	12	36
8	636	133	101	11	29
8,5	543	104	83	8	26
9	456	81	63	6	24
9,5	364	57	48	6	18
10	303	47	35	6	15

			ESTs	ESTs	ESTs
			matching	extending	extending
Tissue	All ESTs	New ESTs	public EST	known	public EST
			closer than	mRNA more	more than 40
			40 bp from beginning	than 40 bp	bp
Brain	329	131	75	3	
Cancerous prostate	134	40	37	3 1	24
Cerebellum	17	9	1	0	6 6
Colon	21	11.	4	0	0
Dystrophic muscle	41	18	8	0	Ý
Fetal brain	70	37	16	0	, i
Fetal kidney	227	116	46	1	1 19
Fetal liver	13	7	2	ó	0
Heart	30	15	7	0	1
Hypertrophic prostate	86	23	22	2	2
Kidney	10	7	3	0	0
Large intestine	21	8	4	Õ	1
Liver	23	9	6	ő	ó
Lung	24	12	4	ŏ	1
Lung (cells)	57	38	6	ő	4
Lymph ganglia	163	60	23	2	12
Lymphocytes	23	6	4	0	2
Muscie	33	16	6	Ö	4
Normal prostate	181	• 61	45	7	11
Ovary	90	57	12	1	2
Pancreas	48	11	6	0	1
Placenta	24	5	1	0	0
Prostate	34	16	4	0	2
Spleen	56	28	10	0	1
Substantia nigra	108	47	27	1	6
Surrenals	15	3	3	1	0
Testis	131	68	25	1	8
Thyroid	17	8	2	0	
Umbilical cord	55	17	12	1	2 3
Uterus	28	15	3	0	2
Non tissue-specific	568	48	177	2	28
Total	2677	947	601	23	150

WO 99/31236 PCT/IB98/02122

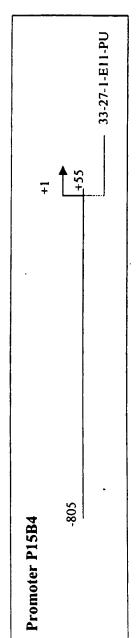




Plasmid name: pED6dpc2 Plasmid size: 5374 bp

8/15

33-30-4-C4-PU Description of promoters structure isolated from SignalTag 5 'ESTs -517 Promoter P13H2



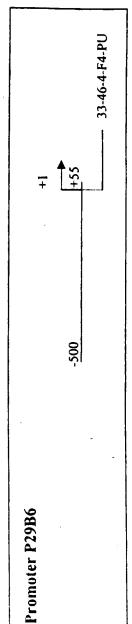


FIGURE 8

WO 99/31236 PCT/IB98/02122

9/15

Description of Transcription Factor Binding Sites present on promoters isolated from SignalTag sequences

Promoter sequence P13H2 (546 bp):

Matrix	Position	Orientation	Score	Length	Sequence
CMYB_01	-502	+	0.983	9	TGTCAGTTG
MYOD_Q6	-501	•	0.961	10	CCCAACTGAC
S8_01	-444	-	0.960	11	AATAGAATTAG
S8_01	-425	+	0.966	11	AACTAAATTAG
DELTAEF1_01	-390		0.960	11	GCACACCTCAG
GATA_C	-364		0.964	11	AGATAAATCCA
CMYB_01	-349	+	0.958	9	CTTCAGTTG
GATA1_02	-343	+	0.959	14	TTGTAGATAGGACA
GATA_C	-339	+	0.953	11	AGATAGGACAT
TAL1ALPHAE47_01	-235	+	0.973	16	CATAACAGATGGTAAG
TAL1BETAE47_01	-235	+	0.983	16	CATAACAGATGGTAAG
TAL1BETAITF2_01	-235	+	0.978	16	CATAACAGATGGTAAG
MYOD_Q6	-232	•	0.954	10	ACCATCTGTT
GATA1_04	-217		0.953	13	TCAAGATAAAGTA
IK1_01	-126	+	0.963	13	AGTTGGGAATTCC
IK2_01	-126	+	0.985	12	AGTTGGGAATTC
CREL_01	-123	+	0.962	10	TGGGAATTCC
GATA1_02	-96	+	0.950	14	TCAGTGATATGGCA
SRY_02	-41	•	0.951	12	TAAAACAAAACA
E2F_02	-33	+	0.957	8	TTTAGCGC
MZF1_01	· -5	•	0.975	8	TGAGGGGA

Promoter sequence P15B4 (861bp):

Matrix	Position	Orientation	Score	Length	Sequence
NFY_Q6	-748	•	0.956	11	GGACCAATCAT
MZF1_01	-738	+	0.962	8	CCTGGGGA
CMYB_01	-684	+	0.994	9	TGACCGTTG
VMYB_02	-682	•	0.985	9	TCCAACGGT
STAT_01	-673	•	0.968	9	TTCCTGGAA
STAT_01	-673	-	0.951	9	TTCCAGGAA
MZF1_01	-556	-	0.956	8	TTGGGGGA
IK2_01	-451	+	0.965	12	GAATGGGATTTC
MZF1_01	-424	+	0.986	8	AGAGGGGA
SRY_02	-398	•	0.955	12	GAAAACAAAACA
MZF1_01	-216	+	0.960	8	GAAGGGGA
MYOD_Q6	-190	+	0.981	10	AGCATCTGCC
DELTAEF1_01	-176	+	0.958 *	11	TCCCACCTTCC
S8_01	5	-	0.992	11	GAGGCAATTAT
MZF1_01	16	•	0.986	8	AGAGGGGA

Promoter sequence P29B6 (555 bp):

Matrix	Position	Orientation	Score	Length	Sequence
ARNT_01	-311	+	0.964	16	GGACTCACGTGCTGCT
NMYC_01	-309	+	0.965	12	ACTCACGTGCTG
USF_01	-309	+	0.985	12	ACTCACGTGCTG
USF_01	-309		0.985	12	CAGCACGTGAGT
NMYC_01	-309		0.956	12	CAGCACGTGAGT
MYCMAX_02	-309		0.972	12	CAGCACGTGAGT
USF_C	-307	' +	0.997	8	TCACGTGC
USF_C	-307	•	0.991	8	GCACGTGA
MZF1_01	-292		0.968	8	CATGGGGA
ELK1_02	-105	+	0.963	14	CTCTCCGGAAGCCT
CETS1P54_01	-102	+	0.974	10	TCCGGAAGCC
AP1_Q4	-42		0.963	11	AGTGACTGAAC
AP1FJ_Q2	-42		0.961	11	AGTGACTGAAC
PADS_C	\ 45	, +	1.000	9	TGTGGTCTC

Figure 9

100.0% identity in 125 aa overlap

70

30 50 40 SEQ ID NO: 217 MADEELEALRRORLAELQAKHGDPGDAAQQEAKHREAEMRNSILAQVLDQSARARLSNLA SEQ ID NO: 516 MADEELEALRRQRLAELQAKHGDPGDAAQQEAKHREAEMRNSILAQVLDQSARARLSNLA 10 20 30 40 70 80 90 100 110 SEQ ID NO: 217 LVKPEKTKAVENYLIQMARYGQLSEKVSEQGLIEILKKVSQQTEKTTTVKFNRRKVMDSD SEQ ID NO: 516 LVKPEKTKAVENYLIQMARYGQLSEKVSEQGLIEILKKVSQQTEKTTTVKFNRRKVMDSD

90

100

80

SEQ ID NO: 217 EDDDY ::::X
SEQ ID NO: 516 EDDDY

CLUSTAL W(1.5) multiple sequence alignment

SEQ	ID N	0: 517	MFCPLKLILLPVLLDYSLGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLS
SEQ	ID N	0: 232	MGCVFQSTEDKCIFKIDWILS
SEQ	ID N	0: 174	MGCVFQSTEDKRIFKIDWILS
SEQ	ID NO	0: 175	MGCVFQSTEDARIFAIDWILS
			******* ** ********
SEQ	ID NO): 517	PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDNLCNDGSLLLQDVQDVE
		0: 232	PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRL
SEO	ID NO): 174	PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDNLCNDGSLLLQDVQEADQGTYICEIRL
SEO	ID NO): 175	PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRL

SEQ	ID NO	517	
SEQ	ID NO): 232	KGESQVFKKAVVLHVLPEEPKGTQMLT
SEQ	ID NO): 174	KGESQVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEE
SEQ	ID NO): 175	KGESQVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAK
-			TAR TO THE TENEDRAL TO THE TEN
SEO			
220	ID NO): 517	
-): 517): 232	
SEQ	ID NO		***************************************
SEQ SEQ	ID NO): 232	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN
SEQ SEQ	ID NO): 232): 174	***************************************
SEQ SEQ	ID NO): 232): 174	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN
SEQ SEQ SEQ	ID NO): 232): 174	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN
SEQ SEQ SEQ	ID NO): 232): 174): 175	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN VTRRKHHCVREGSG
SEQ SEQ SEQ SEQ	ID NO ID NO ID NO ID NO	0: 232 0: 174 0: 175	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN VTRRKHHCVREGSG
SEQ SEQ SEQ SEQ SEQ	ID NO ID NO ID NO ID NO ID NO	0: 232 0: 174 0: 175 0: 517 0: 232	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN VTRRKHHCVREGSG
SEQ SEQ SEQ SEQ SEQ	ID NO ID NO ID NO ID NO ID NO	0: 232 0: 174 0: 175 0: 517 0: 232 0: 174	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN VTRRKHHCVREGSG
SEQ SEQ SEQ SEQ SEQ SEQ SEQ	ID NO ID NO ID NO ID NO ID NO	0: 232 0: 174 0: 175 0: 517 0: 232 0: 174 0: 175	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN VTRRKHHCVREGSG
SEQ SEQ SEQ SEQ SEQ SEQ	ID NO ID NO ID NO ID NO ID NO ID NO	0: 232 0: 174 0: 175 0: 517 0: 232 0: 174 0: 175	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN VTRRKHHCVREGSG
SEQ SEQ SEQ SEQ SEQ SEQ SEQ	ID NO	0: 232 0: 174 0: 175 0: 517 0: 232 0: 174 0: 175	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN VTRRKHHCVREGSG
SEQ SEQ SEQ SEQ SEQ SEQ SEQ SEQ SEQ	ID NO	0: 232 0: 174 0: 175 0: 517 0: 232 0: 174 0: 517 0: 517 0: 232 0: 174	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN VTRRKHHCVREGSG
SEQ SEQ SEQ SEQ SEQ SEQ SEQ SEQ SEQ	ID NO	0: 232 0: 174 0: 175 0: 517 0: 232 0: 174 0: 175	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN VTRRKHHCVREGSG

99.6	5 % :	ident	ity	in 2	25 a	aa ov	erlap									
				10		20		30		40		50	ı	60	כ	
SEQ	ID	NO:	515	PTAV	QKE	EARQD'	VEALLS	RTVR	TOILI	GKELR	VATQE	ŒGSS	GRCML	TLLG	LSFILA	GLI
222																
SEQ	ענ	NO:	231							n.	VAIQE	10	GRUML	20	LSFILA	30
														20		30
				70		80		90		100		110)	120	5	
SEQ	ID	NO:	515	VGGA	CIY	KYFMP:	KSTIYE	RGEMC	FFDSE	DPANS	LRGGE	NFLF	VTEEA	DIRE	DDNIAI	IDV
				::::	:::	::::	::::::	::::	:::::	:::::	:::::	::::	:::::	::::	:::::	:::
SEQ	ID	NO:	231	VGGA	CIY		KSTIYE		FFDSE		LRGGE		VTEEA		DDNIAI	
						40		50		60		70		80		90
			,	130		140		150		160		170	١	180	n	
650	*5	MO:			ren:		ומחעדד		זרו.זע מ						FGKLAS	CRV
250	ענ	NO:	313				::::::					: : : : :	::::::	::::	:::::	:::
SEO	ID	NO:	231								YLMPL	NTSIV	MPPKN	ILVEL	FGKLAS	GRY
						100		110		120		130		140		150
			_	190		200		210		220		230	•	24	-	
SEQ	ID	NO:	515	LPQT	YVV	REDLV.	AVEEI	RDVSN	LGIF	AOPCM	INRKSFI	RLRRE	SDLLLG	FNKR	AIDKCW	KIR
				::::	;;;	:::::	:::::: *******************************	: : : : :	:::::	COLON	::::::	:::::	::::::	PNVD	::::: * TDYCW	:::: VTD
SEQ	ΙD	NO:	23 I	PPQT		KEDLY. 160		KDVSN 170	DOIF.	180		190	(DILLIC	200	AIDKCW	210
						100	•	170		100	•	150		200		210
			2	250		260										
SEQ	ID	NO:	515	HFPN	EFI'	VETKI	CQE									
_				::::	:::	::::	:::									
SEQ	ID	NO:	231	HFPN	EFI	VETKI	CQE									
						220										

WO 99/31236 PCT/IB98/02122

13/15

99.7% identity in 353 aa overlap MERGLKSADPRDGTGYTGWAGIAVLYLHLY SEQ ID NO:196 SEQ ID NO:518 LAEGYFDAAGRLTPEFSQRLTNKIRELLQQMERGLKSADPRDGTGYTGWAGIAVLYLHLY SEQ ID NO: 196 DVFGDPAYLQLAHGYVKQSLNCLTKRSITFLCGDAGPLAVAAVLYHKMNNEKQAEDCITR SEQ ID NO:518 DVFGDPAYLQLAHGYVKQSLNCLTKRSITFLCGDAGPLAVAAVLYHKMNNEKOAEDCITR SEQ ID NO: 196 LIHLNKIDPHAPNEMLYGRIGYIYALLFVNKNFGVEKTPQSHIQQICETILTSGENLARK SEQ ID NO:518 LIHLNKIDPHAPNEMLYGRIGYIYALLFVNKNFGVEKIPQSHIQQICETILTSGENLARK 180 1 SEQ ID NO:196 RNFTAKSPLMYEWYQEYYVGAAHGLAGIYYYLMQPSLQVSQGKLHSLVKPSVDYVCOLKF SEQ ID NO:518 RNFTAKSPLMYEWYQEYYVGAAHGLAGIYYYLMQPSLQVSQGKLHSLVKPSVDYVCQLKF · 210 SEQ ID NO:196 PSGNYPPCIGDNRDLLVHWCHGAPGVIYMLIQAYKVFREEKYLCDAYQCADVIWQYGLLK SEQ ID NO:518 PSGNYPPCIGDNRDLLVHWCHGAPGVIYMLIQAYKVFREEKYLCDAYQCADVIWQYGLLK SEQ ID NO:196 KGYGLCHGSAGNAYAFLTLYNLTQDMKYLYRACKFAEWCLEYGEHGCRTPDTPFSLFEGM SEQ ID NO:518 KGYGLCHGSAGNAYAFLTLYNLTQDMKYLYRACKFAEWCLEYGEHGCRTPDTPFSLFEGM SEQ ID NO:196 AGTIYFLADLLVPTKARFPAFEL SEQ ID NO:518 AGTIYFLADLLVPTKARFPAFEL

98.5% identity in 194 aa overlap SEQ ID NO:519 ARNLPPLTDAQKNKLRHLSVVTLAAKVKCIPYAVLLEALALRNVRQLEDLVIEAVYADVL SEQ ID NO:158 ARNLPPLTEAQKNKLRHLSVVTLAAKVKCIPYAVLLEALALRNVRQLEDLVIEAVYADVL SEQ ID NO:519 RGSLDQRNQRLEVDYSIGRDIQRQDLSAIAQTLQEWCVGCEVVLSGIEEQVSRANQHKEQ SEQ ID NO:158 RGSLDQRNQRLEVDYSIGRDIQRQDLSAIARTLQEWCVGCEVVLSGIEEQVSRANQHKEQ SEQ ID NO:519 QLGLKQQIESEVANLKKTIKVTTAAAAAATSQDPEQHLTELREPASGTNQRQPSKKASKG SEQ ID NO:158 QLGLKQQIESEVANLKKTIKVTTAAAAAATSQDPEQHLTELREPAPGTNQRQPSKKASKG SEQ ID NO:519 KGLRGSAKIWSKSN SEQ ID NO:158 KGLRGSAKIWSKSN 88.7% identity in 62 aa overlap SEQ ID NO:519 MSAEVKVTGQNQEQFLLLAKSAKGAALATLIHQVLEAPGVYVFGELLDMPNVRELAESDF SEQ ID NO:158 MSAEVKVTGQNQEQFLLLAKSAKGAALATLIHQVLEAPGVYVFGELLDMPNVRELXARNL SEQ ID NO:519 AS

SEQ ID NO:158 PP

WO 99/31236 PCT/IB98/02122

15/15

68.	9 8	identit	y 111 /4 (aa Overia	яр				
				10	20	30	40	50	
SEQ	ID	NO:226	MIARRN	PVPLRFLPI	DEARSLPPP	KLTDPRLLYIC	GFLGYCSGLI	DNLIRRRPIA	TAGLHE
			: :	: : : :		:::::::	::::::::::	:: :::::	:::::
SEQ	ID	NO:514	MMTGRQGI	RATFQFLPI	DEARSLPPP	KLTDPRLAFVO	GFLGYCSGLI	DNAIRRRPVL	LAGLHR
				10	20	30	40	. 50	60
			50	70					
SEQ	ID	NO:226	QLLYITA	FFLLDIIL					
SEQ	ID	NO:514	QLLYITS	FVFVGYYLI	KRODYMYA	VRDHDMFSYI	SHPEDFPEK	DKKTYGEVFE	EFHPVR
			•	70	80	90	100	110	120

FIGURE 15

-1-WO 99/31236 PCT/IB98/02122 <110> Dumas Milne Edwards, Jean-Baptiste Duclert, Aymeric Bougueleret, Lydie <120> Extended cDNAS for Secreted Proteins <130> GENSET.019A <160> 519 <170> Patent.pm <210> 1 <211> 47 <212> RNA <213> Artificial Sequence <220> <221> In vitro transcription product <221> modified_base <222> (1)...(1) <223> m7g ngcauccuae ucccauccaa uuccacccua acuccuccca ucuccac 47 <210> 2 <211> 46 <212> RNA <213> Artificial Sequence <220> <223> In vitro transcription product gcauccuacu cccauccaau uccacccuaa cuccucccau cuccac 46

<210> 3
<211> 25
<212> DNA
<213> Artificial Sequence
<220>
<223> In vitro transcription product
<400> 3
atcaagaatt cgcacgagac catta

25

<210> 4 <211> 25 <212> DNA <213> Artificial Sequence <210> 5 <211> 25 <212> DNA <213> Artificial Sequence <220> <223> Oligonucleotide <400> 5 ccgacaagac caacgtcaag gccgc

<210> 6 <211> 25 <212> DNA <213> Artificial Sequence <220> <223> Oligonucleotide <400> 6

25

25

<210> 7 <211> 25 <212> DNA <213> Artificial Sequence <220> <223> Oligonucleotide <400> 7 25

<210> 8 <211> 25 <212> DNA <213> Artificial Sequence <223> Oligonucleotide 25 gcttggtctt gttctggagt ttaga

<210> 9

tcaccagcag gcagtggctt aggag

agtgattcct gctactttgg atggc

WO 99/31236	-3-	PCT/IB98/0212
211> 25		
212> DNA		
213> Artificial Sequence		
220> · 223> Oligonucleotide		•
400> 9		25
ccagaatgg gagacaagcc aattt		2-
210> 10		
211> 25		
212> DNA		,
213> Artificial Sequence		
220>		
223> Oligonucleotide		
400> 10		25
gggaggagg aaacagcgtg agtcc		
210> 11		
:211> 25		
:212> DNA :213> Artificial Sequence		
<220>		
223> Oligonucleotide		
<400> 11		25
atgggaaagg aaaagactca tatca		23
<210> 12		
<211> 25		
<212> DNA		
<213> Artificial Sequence	•	
<220>		
<223> Oligonucleotide		
<400> 12		25
agcagcaaca atcaggacag cacag		
<210> 13		
<211> 25		
<212> DNA		
<213> Artificial Sequence		
<220>		
<223> Oligonucleotide		

25

<400> 13 atcaagaatt cgcacgagac catta

```
<210> 14
<211> 67
<212> DNA
<213> Artificial Sequence
<223> Oligonucleotide
<400> 14
atogttgaga ctcgtaccag cagagtcacg agagagacta cacggtactg gttttttttt
                                                                       60
                                                                       67
tttttvn
<210> 15
<211> 29
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide
<400> 15
                                                                       29
ccagcagagt cacgagagag actacacgg
<210> 16
<211> 25
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide
<400> 16
                                                                        25
cacgagagag actacacggt actgg
<210> 17
<211> 526
<212> DNA
<213>. Homo sapiens
<220>
<221> misc_feature
<222> complement(261..376)
<223> blastn
<221> misc_feature
<222> complement (380..486)
<223> blastn
<221> misc_feature
<222> complement(110..145)
<223> blastn
<221> misc_feature
<222> complement (196..229)
<223> blastn
```

<221> sig_peptide <222> 90..140 <223> Von Heijne matrix aatatrarac agctacaata ttccagggcc artcacttgc catttctcat aacagcgtca 60 gagagaaaga actgactgar acgtttgag atg aag aaa gtt ctc ctc ctg atc 113 Met Lys Lys Val Leu Leu Leu Ile -15 aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag 161 Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln 1 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr 209 Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 20 15 10 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att 257 Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 35 30 cca ttt cca aga ttt cca tgg ttt aga cgt aan ttt cct att cca ata 305 Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Xaa Phe Pro Ile Pro Ile 45 50 cet gaa tet gee eet aca act eee ett eet age gaa aag taaacaaraa 354 Pro Glu Ser Ala Pro Thr Thr Pro Leu Pro Ser Glu Lys 60 ggaaaagtca crataaacct ggtcacctga aattgaaatt gagccacttc cttgaaraat 414 caaaattoot gttaataaaa raaaaacaaa tgtaattgaa atagcacaca gcattotota 474 526 <210> 18 <211> 17 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> 1..17 <223> Von Heijne matrix score 8.2 seq LLLITAILAVAVG/FP <400> 18 Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val 10 5 1 Gly <210> 19 <211> 822 <212> DNA <213> Homo sapiens <221> misc_feature <222> 260..464 <223> blastn <221> misc feature <222> 118..184

WO 99/31236 PCT/IB98/02122

<223> blastn	
<221> misc feature	
<222> 56113	
<223> blastn	
<221> misc feature	
<222> 454485	
<223> blastn	
<221> misc_feature	
<222> 118545	
<223> blastn	
<221> misc feature	
<222> 65369	
<223> blastn	
<221> misc feature	
<222> 61. 399	
<223> blastn	
<221> misc_feature	
<222> 408458	
<223> blastn	
<221> misc_feature	
<222> 60399	
<223> blastn	
<221> misc feature	
<222> 393432	
<223> blastn	
<221> sig_peptide	
<222> 346408	
<223> Von Heijne matrix	
<400> 19	
actectitta geatagggge tieggegeea geggeeageg etagteggte tggtaagtge	60
ctgatgccga gttccgtctc tcgcgtcttt tcctggtccc aggcaaagcg gasgnagatc	120
ctcaaacggc ctagtgcttc gcgcttccgg agaaaatcag cggtctaatt aattcctctg	180
qtttqttqaa qcaqttacca agaatettca aceetttece acaaaageta attgagtaca	240
cgttcctgtt gagtacacgt tcctgttgat ttacaaaagg tgcaggtatg agcaggtctg	300
aagactaaca ttttgtgaag ttgtaaaaca gaaaacctgt tagaa atg tgg tgt tt	35
Met Trp Trp Phe	
-20	
cag caa ggc ctc agt ttc ctt cct tca gcc ctt gta att tgg aca tct	40
Gln Gln Gly Leu Ser Phe Leu Pro Ser Ala Leu Val Ile Trp Thr Ser	
-15 -10 -5	
get get the ata the tea tac att act gea gea aca etc cae cat ata	45
Ala Ala Phe Ile Phe Ser Tyr Ile Thr Ala Val Thr Leu His His Ile	
1 5 10 15	
gae eeg get tta eet tat ate agt gae aet ggt aca gta get eea raa	50
Asp Pro Ala Leu Pro Tyr Ile Ser Asp Thr Gly Thr Val Ala Pro Xaa	
20 25 30	
aaa tgc tta ttt ggg gca atg cta aat att gcg gca gtt tta tgt caa	54
Lys Cys Leu Phe Gly Ala Met Leu Asn Ile Ala Ala Val Leu Cys Gln	
35 40 45	_
aaa tagaaatcag gaarataatt caacttaaag aakttcattt catgaccaaa	60
Lys	
crotroara, acatorort acaagcatar crotrotatt gottroraca ctgttgaatt	66

-7-WO 99/31236 PCT/IB98/02122

gtctggcaat atttctgcag tggaaaattt gatttarmta gttcttgact gataaatatg gtaaggtggg cttttccccc tgtgtaattg gctactatgt cttactgagc caagttgtaw tttgaaataa aatgatatga gagtgacaca aaaaaaaaaa	722 782 822
<210> 20 <211> 21 <212> PRT <213> Homo sapiens	
<220> <221> SIGNAL <222> 121 <223> Von Heijne matrix score 5.5 seq SFLPSALVIWTSA/AF	
<pre>c400> 20 Met Trp Trp Phe Gln Gln Gly Leu Ser Phe Leu Pro Ser Ala Leu Val 1</pre>	
<210> 21 <211> 405 <212> DNA <213> Homo sapiens	
<220> <221> misc_feature <222> complement(103398) <223> blastn	
<221> sig_peptide <222> 185295 <223> Von Heijne matrix	
<400> 21 atcacettet tetecateet tstetgggee agteeceare ceagteecte teetgacetg eccageecaa gteageette ageaegeget tttetgeaca cagatattee aggeetaeet ggeatteeag gaceteegma atgatgetee agteeettae aagegettee tggatgaggg tgge atg gtg etg ace ace ete eee ttg eee tet gee aac age eet gtg Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val -35 -30 -25	60 120 180 229
aac atg ccc acc act ggc ccc aac agc ctg agt tat gct agc tct gcc Asn Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala -20 -15 -10	277
ctg tcc ccc tgt ctg acc gct cca aak tcc ccc cgg ctt gct atg atg Leu Ser Pro Cys Leu Thr Ala Pro Xaa Ser Pro Arg Leu Ala Met Met -5 1 5 10	325
cct gac aac taaatatcct tatccaaatc aataaarwra raatcctccc Pro Asp Asn	374
tccaraaggg tttctaaaaa caaaaaaaa a	40

<210> 22 <211> 37 <212> PRT

WO 99/31236 -8- PCT/IB98/02122

```
<213> Homo sapiens
<220>
<221> SIGNAL
<222> 1..37
<223> Von Heijne matrix
     score 5.9
      seq LSYASSALSPCLT/AP
Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val Asn
                                   10
Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala Leu
            20
                                25
Ser Pro Cys Leu Thr
        35
<210> 23
<211> 496
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> 149..331
<223> blastn
<221> misc_feature
<222> 328..485
<223> blastn
<221> misc_feature
<222> complement (182..496)
<223> blastn
<221> sig_peptide
<222> 196..240
<223> Von Heijne matrix
<400> 23
aaaaaattgg tcccagtttt caccetgeeg cagggetgge tgggggaggge ageggtttag
                                                                      120
attagccgtg gcctaggccg tttaacgggg tgacacgagc ntgcagggcc gagtccaagg
cccggagata ggaccaaccg tcaggaatgc gaggaatgtt tttcttcgga ctctatcgag
                                                                      180
                                                                      231
gcacacagac agacc atg ggg att ctg tct aca gtg aca gcc tta aca ttt
                 Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe
                                      -10
                  -15
gcc ara gcc ctg gac ggc tgc aga aat ggc att gcc cac cct gca agt
                                                                      279
Ala Xaa Ala Leu Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser
                                                10
gag aag cac aga ctc gag aaa tgt agg gaa ctc gag asc asc cac tcg
                                                                       327
Glu Lys His Arg Leu Glu Lys Cys Arg Glu Leu Glu Xaa Xaa His Ser
                                             25
                         20
                                                                       375
gcc cca gga tca acc cas cac cga aga aaa aca acc aga aga aat tat
Ala Pro Gly Ser Thr Xaa His Arg Arg Lys Thr Thr Arg Arg Asn Tyr
                     35
                                                              45
                                                                       424
tot toa goo tgaaatgaak cogggatcaa atggttgctg atcaragcco
 Ser Ser Ala
 atatttaaat tggaaaagtc aaattgasca ttattaaata aagcttgttt aatatgtctc
                                                                       484
                                                                       496
 aaacaaaaaa aa
```

WO 99/31236 -9- PCT/IB98/02122

```
<210> 24
<211> 15
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> 1..15
<223> Von Heijne matrix
      score 5.5
      seq ILSTVTALTFAXA/LD
Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe Ala Xaa Ala
                                    10
<210> 25
<211> 623
<212> DNA
<213> Homo sapiens
<220>
<221> sig_peptide
<222> 49..96
<223> Von Heijne matrix
<400> 25°
aaagateeet geageeegge aggagagaag getgageett etggegte atg gag agg
                                                                       57
                                                     Met Glu Arg
ctc gtc cta acc ctg tgc acc ctc ccg ctg gct gtg gcg tct gct ggc
                                                                      105
Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala Ser Ala Gly
                                 - 5
            -10
 tgc gcc acg acg cca gct cgc aac ctg agc tgc tac cag tgc ttc aag
                                                                      153
 Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln Cys Phe Lys
                                            15
                        10
                                                                      201
 gtc agc agc tgg acg gag tgc ccg ccc acc tgg tgc agc ccg ctg gac
 Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser Pro Leu Asp
                                         30
                     25
 caa gtc tgc atc tcc aac gag gtg gtc gtc tct ttt aaa tgg agt gta
                                                                       249
 Gln Val Cys Ile Ser Asn Glu Val Val Val Ser Phe Lys Trp Ser Val
                                     45
                40
 ege gte etg etc age aaa ege tgt get eec aga tgt eec aac gae aac
 Arg Val Leu Leu Ser Lys Arg Cys Ala Pro Arg Cys Pro Asn Asp Asn
                                 60
            55
 atg aak ttc gaa tgg tcg ccg gcc ccc atg gtg caa ggc gtg atc acc
                                                                       345
 Met Xaa Phe Glu Trp Ser Pro Ala Pro Met Val Gln Gly Val Ile Thr
                                                 80
         70
                                                                       393
 agg cgc tgc tgt tcc tgg gct ctc tgc aac agg gca ctg acc cca cag
 Arg Arg Cys Cys Ser Trp Ala Leu Cys Asn Arg Ala Leu Thr Pro Gln
                                              95
 gag ggg ege tgg gee etg era ggg ggg etc etg etc eag gae eet teg
                                                                       441
 Glu Gly Arg Trp Ala Leu Xaa Gly Gly Leu Leu Gln Asp Pro Ser
                     105
                                         110
 agg ggc ara aaa acc tgg gtg cgg cca cag ctg ggg ctc cca ctc tgc
                                                                       489
 Arg Gly Xaa Lys Thr Trp Val Arg Pro Gln Leu Gly Leu Pro Leu Cys
                 1,50
                                     125
 ctt ecc awt tee aac ecc etc tge eca rgg gaa acc eag gaa gga
                                                                        534
```

WO 99/31236 -10 - PCT/IB98/02122

Leu Pro Xaa Ser Asn Pro Leu Cys Pro Xaa Glu Thr Gln Glu Gly

140 135 taacactgtg ggtgccccca cctgtgcatt gggaccacra cttcaccctc ttggaracaa 594 623 taaactctca tgcccccaaa aaaaaaaaa <210> 26 <211> 16 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> 1..16 <223> Von Heijne matrix score 10.1 seq LVLTLCTLPLAVA/SA <400> 26 Met Glu Arg Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala <210> 27 <211> 848 <212> DNA <213> Homo sapiens <220> <221> sig_peptide <222> 32..73 <223> Von Heijne matrix <400> 27 52 aactttgeet tgtgttttee accetgaaag a atg ttg tgg etg ete ttt ttt. Met Leu Trp Leu Leu Phe Phe -10 ctg gtg act gcc att cat gct gaa ctc tgt caa cca ggt gca gaa aat 100 Leu Val Thr Ala Ile His Ala Glu Leu Cys Gln Pro Gly Ala Glu Asn get ttt aaa gtg aga ett agt ate aga aca get etg gga gat aaa gea 148 Ala Phe Lys Val Arg Leu Ser Ile Arg Thr Ala Leu Gly Asp Lys Ala 20 15 tat gcc tgg gat acc aat gaa gaa tac ctc ttc aaa gcg atg gta gct 196 Tyr Ala Trp Asp Thr Asn Glu Glu Tyr Leu Phe Lys Ala Met Val Ala 35 30 tto too atg aga aaa gtt coc aac aga gaa goa aca gaa att too cat 244 Phe Ser Met Arg Lys Val Pro Asn Arg Glu Ala Thr Glu Ile Ser His 50 45 gto ota ott tgo aat gta acc cag agg gta toa tto tgg ttt gtg gtt 292 Val Leu Leu Cys Asn Val Thr Gln Arg Val Ser Phe Trp Phe Val Val 70 65 aca gac cet tea aaa aat cae ace ett eet get gtt gag gtg caa tea 340 Thr Asp Pro Ser Lys Asn His Thr Leu Pro Ala Val Glu Val Gln Ser 85 75 80 388 gee ata aga atg aac aag aac egg ate aac aat gee tte ttt eta aat Ala Ile Arg Met Asn Lys Asn Arg Ile Asn Asn Ala Phe Phe Leu Asn 100 95 gac caa act ctg gaa ttt tta aaa atc cct tcc aca ctt gca cca ccc Asp Gln Thr Leu Glu Phe Leu Lys Ile Pro Ser Thr Leu Ala Pro Pro

				110					115					120		
atg	gac	cca	tct	gtg	CCC	atc	tgg	att	att	ata	ttt	ggt	gtg	ata	ttt	484
Met	Asp	Pro		Val	Pro	Ile	Trp		Ile	Ile	Phe	Gly		Ile	Phe	
			125					130					135			
				_	-		gca									532
Cys	Ile		Ile	Val	Ala	Ile	Ala	Leu	Leu	Ile	Leu		Gly	Ile	Trp	
		140					145					150				
							gaa									580
Gln		Xaa	Xaa	Lys	Asn	Lys	Glu	Pro	Ser	Glu	Val	Asp	Asp	Ala	Glu	
	155					160					165					
rat	aak	tgt	gaa	aac	atg	atc	aça	att	gaa	aat	ggc	atc	CCC	tct	gat	628
Xaa	Xaa	Cys	Glu	Asn	Met	Ile	Thr	Ile	Glu	Asn	Gly	Ile	Pro	Ser	Asp	
170					175					180					185	
CCC	ctg	gac	atg	aag	gga	999	cat	att	aat	gat	gcc	ttc	atg	aca	gag	676
Pro	Leu	Asp	Met	Lys	Gly	Gly	His	Ile	Asn	qzA	Ala	Phe	Met	Thr	Glu	
				190					195					200		
gat	gag	agg	ctc	acc	cct	ctc	tgaa	ıgggc	tg t	tgtt	ctg	t to	ctca	araa	ì	727
Asp	Glu	Arg	Leu	Thr	Pro	Leu										
			205													
atta	aaca	itt t	gttt	ctgt	g tg	acto	jctga	gca	tcct	gaa	atac	caaq	gag d	agat	catat	787
wttt	tgtt	tc a	ccat	tctt	c tt	ttgt	aata	aat	tttg	gaat	gtg	ettga	aaa a	aaaa	aaaaa	847
C																848

<210> 28

<211> 14 <212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> 1..14

<223> Von Heijne matrix score 10.7 seq LWLLFFLVTAIHA/EL

<400> 28

Met Leu Trp Leu Leu Phe Phe Leu Val Thr Ala Ile His Ala

<210> 29

<211> 25

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 29

gggaagatgg agatagtatt gcctg

25

<210> 30

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> Olignucleotide

<400> 30 ctgccatgta catgatagag agattc

26

- <210> 31
- <211> 546
- <212> DNA
- <213> Homo sapiens
- <220>
- <221> promoter
- <222> 1..517
- <221> transcription start site
- <222> 518
- <221> protein_bind
- <222> 17..25
- <223> matinspector prediction name CMYB_01 score 0.983 sequence tgtcagttg
- <221> protein bind
- <222> complement(18..27)
- <223> matinspector prediction name MYOD_Q6 score 0.961 sequence cccaactgac
- <221> protein_bind
- <222> complement(75..85)
- <223> matinspector prediction name S8 01 score 0.960 sequence aatagaattag
- <221> protein_bind
- <222> 94..104
- <223> matinspector prediction name S8_01 score 0.966 sequence aactaaattag
- <221> protein_bind
- <222> complement(129..139)
- <223> matinspector prediction name DELTAEF1_01 score 0.960 sequence gcacacctcag
- <221> protein_bind
- <222> complement(155..165)
- <223> matinspector prediction name GATA_C score 0.964 sequence agataaatcca
- <221> protein_bind

- <222> 170..178
- <223> matinspector prediction
 name CMYB_01
 score 0.958
 sequence cttcagttg
- <221> protein_bind
- <222> 176..189
- <223> matinspector prediction name GATA1_02 score 0.959 sequence ttgtagataggaca
- <221> protein_bind
- <222> 180..190
- <223> matinspector prediction
 name GATA_C
 score 0.953
 sequence agataggacat
- <221> protein_bind
- <222> 284..299
- <223> matinspector prediction name TAL1ALPHAE47_01 score 0.973 sequence cataacagatggtaag
- <221> protein_bind
- <222> 284..299
- <223> matinspector prediction name TAL1BETAE47_01 score 0.983 sequence cataacagatggtaag
- <221> protein bind
- <222> 284..299
- <223> matinspector prediction
 name TAL1BETAITF2_01
 score 0.978
 sequence cataacagatggtaag
- <221> protein bind
- <222> complement(287..296)
- <223> matinspector prediction
 name MYOD_Q6
 score 0.954
 sequence accatctgtt
- <221> protein bind
- <222> complement (302..314)
- <223> matinspector prediction name GATA1_04 score 0.953 sequence tcaagataaagta
- <221> protein_bind
- <222> 393..405
- <223> matinspector prediction name IK1_01 score 0.963 sequence agitgggaattcc

WO 99/31236 -14 - PCT/IB98/02122

```
<221> protein_bind
<222> 393..404
<223> matinspector prediction
      name IK2_01
      score 0.985
      sequence agttgggaattc
<221> protein bind
<222> 396..405
<223> matinspector prediction
      name CREL 01
      score 0.962
      sequence tgggaattcc
<221> protein bind
<222> 423..436
<223> matinspector prediction
      name GATA1 02
      score 0.950
      sequence tcagtgatatggca,
<221> protein bind
<222> complement (478..489)
<223> matinspector prediction
      name SRY 02
      score 0.951
      sequence taaaacaaaca
<221> protein_bind
<222> 486..493
<223> matinspector prediction
      name E2F 02
      score 0.957
      sequence tttagcgc
<221> protein_bind
<222> complement (514..521)
<223> matinspector prediction
      name MZF1 01
      score 0.975
      sequence tgagggga
<400> 31
                                                                       60
tgagtgcagt gttacatgtc agttgggtta agtttgttaa tgtcattcaa atcttctatg
tottgatttg cotgotaatt ctattattto tggaactaaa ttagtttgat ggttotatta
gttattgact gaggtgtgct aatctcccat tatgtggatt tatctatttc ttcagttgta
gataggacat tgatagatac ataagtacca ggacaaaagc agggagatct tttttccaaa
                                                                      240
                                                                      300
atcaggagaa aaaaatgaca tctggaaaac ctatagggaa aggcataaca gatggtaagg
                                                                      360
atactttatc ttgagtagga gagccttcct gtggcaacgt ggagaaggga agaggtcgta
                                                                      420
gaattgagga gtcagctcag ttagaagcag ggagttggga attccgttca tgtgatttag
                                                                      480
catcagtgat atggcaaatg tgggactaag ggtagtgatc agagggttaa aattgtgtgt
trigitting cyclotygy grategeett gggtcccctc aaacagattc ccatgaatct
                                                                      540
                                                                      546
cttcat
```

<210> 32

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 32 gtaccaggga ctgtgaccat tgc

23

<210> 33

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<400> 33

ctgtgaccat tgctcccaag agag

24

<210> 34

<211> 861

<212> DNA

<213> Homo sapiens

<220>

<221> promoter

<222> 1..806

<221> transcription start site

<222> 807

<221> protein_bind

<222> complement (60..70)

<223> matinspector prediction name NFY_Q6 score 0.956 sequence ggaccaatcat

<221> protein_bind

<222> 70..77

<223> matinspector prediction name MZF1_01 score 0.962 sequence cctgggga

<221> protein_bind

<222> 124..132

<223> matinspector prediction name CMYB_01 score 0.994 sequence tgaccgttg

<221> protein_bind

<222> complement (126..134)

<223> matinspector prediction name VMYB_02 score 0.985 sequence tccaacggt

<221> protein_bind

<222> 135..143

WO 99/31236 -16- PCT/IB98/02122

- <223> matinspector prediction
 name STAT_01
 score 0.968
 sequence ttcctggaa
- <221> protein_bind
- <222> complement (135..143)
- <223> matinspector prediction name STAT_01 score 0.951 sequence ttccaggaa
- <221> protein bind
- <222> complement (252..259)
- <223> matinspector prediction name M2F1_01 score 0.956 sequence ttggggga
- <221> protein_bind
- <222> 357..368
- <223> matinspector prediction name IK2_01 score 0.965 sequence gaatgggatttc
- <221> protein_bind
- <222> 384..391
- <223> matinspector prediction name MZF1_01 score 0.986 sequence agagggga
- <221> protein_bind
- <222> complement (410..421)
- <223> matinspector prediction name SRY_02 score 0.955 sequence gaaaacaaaaca
- <221> protein bind
- <222> 592..599
- <223> matinspector prediction name MZF1_01 score 0.960 sequence gaagggga
- <221> protein_bind
- <222> 618..627
- <223> matinspector prediction name MYOD_Q6 score 0.981 sequence agcatctgcc
- <221> protein_bind
- <222> 632..642
- <223> matinspector prediction
 name DELTAEF1_01
 score 0.958
 sequence tcccaccttcc
- <221> protein_bind

```
<222> complement (813..823)
<223> matinspector prediction
     name S8_01
     score 0.992
     sequence gaggcaattat
<221> protein_bind
<222> complement(824..831)
<223> matinspector prediction
     name MZF1 01
     score 0.986
     sequence agagggga
<400> 34
tactataggg cacgcgtggt cgacggccgg gctgttctgg agcagagggc atgtcagtaa
                                                                60
tgattggtcc ctggggaagg tctggctggc tccagcacag tgaggcattt aggtatctct
                                                               120
180
ctcagagggc taggcacgag ggaaggtcag aggagaaggs aggsarggcc cagtgagarg
                                                               240
ggagcatgcc ttcccccaac cctggcttsc ycttggymam agggcgktty tgggmacttr
                                                               300
aaytcagggc ccaascagaa scacaggccc aktcntggct smaagcacaa tagcctgaat
                                                               360
420
ccaaatcaag gtaacttgct cccttctgct acgggccttg gtcttggctt gtcctcaccc
                                                               480
agtoggaact coctacoact ttoaggagag tggttttagg cocgtggggc tgttotgtto
                                                               540
caagcagtgt gagaacatgg ctggtagagg ctctagctgt gtgcggggcc tgaaggggag
                                                               600
tgggttctcg cccaaagagc atctgcccat ttcccacctt cccttctccc accagaagct
                                                               660
tgcctgagct gtttggacaa aaatccaaac cccacttggc tactctggcc tggcttcagc
                                                               720
ttggaaccca atacctaggc ttacaggcca tcctgagcca ggggcctctg gaaattctct
                                                               780
tectgatggt cetttaggtt tgggcacaaa atataattge eteteceete teccatttte
                                                               840
tctcttggga gcaatggtca c
                                                               861
<210> 35
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide
<400> 35
                                                                 20
ctgggatgga aggcacqqta
<210> 36
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide
<400> 36
                                                                 20
gagaccacac agctagacaa
<210> 37
<211> 555
```

<212> DNA

<213 > Homo sapiens

- <220> <221> promoter <222> 1..500 <221> transcription start site <222> 501 <221> protein_bind <222> 191..206 <223> matinspector prediction name ARNT_01 score 0.964 sequence ggactcacgtgctgct <221> protein_bind <222> 193..204 <223> matinspector prediction name NMYC 01 score 0.965 sequence actcacgtgctg <221> protein_bind <222> 193..204 <223> matinspector prediction name USF 01 score 0.985 sequence actcacgtgctg <221> protein_bind <222> complement(193..204) <223> matinspector prediction name USF_01 score 0.985 sequence cagcacgtgagt <221> protein_bind <222> complement(193..204) <223> matinspector prediction name NMYC_01 score 0.956 sequence cagcacgtgagt <221> protein_bind <222> complement(193..204) <223> matinspector prediction name MYCMAX_02 score 0.972 sequence cagcacgtgagt <221> protein_bind <222> 195..202 <223> matinspector prediction name USF C
- <221> protein_bind <222> complement(195..202) <223> matinspector prediction name USF_C score 0.991

sequence tcacgtgc

score 0.997

WO 99/31236 -19- PCT/IB98/02122

sequence gcacgtga

- <221> protein_bind
- <222> complement (210..217)
- <223> matinspector prediction name MZF1_01 score 0.968 sequence catgggga
- <221> protein_bind
- <222> 397..410
- <223> matinspector prediction name ELK1_02 score 0.963 sequence ctctcggaagcct
- <221> protein bind
- <222> 400..409
- <223> matinspector prediction name CETS1P54_01 score 0.974 sequence tccggaagcc
- <221> protein_bind
- <222> complement (460..470)
- <223> matinspector prediction name API_Q4 score 0.963 sequence agtgactgaac
- <221> protein bind
- <222> complement(460..470)
- <223> matinspector prediction name APIFJ_Q2 score 0.961 sequence agtgactgaac
- <221> protein bind
- <222> 547..555
- <223> matinspector prediction name PADS_C score 1.000 sequence tgtggtctc
- <400> 37 ctatagggca cgcktggtcg acggcccggg ctggtctggt ctgtkgtgga gtcgggttga 60 aggacageat ttgtkacate tggtetactg cacetteect etgeegtgea ettggeettt 120 180 kawaagetca geaceggtge ceateacagg geeggeagea cacacatece attacteaga 240 aggaactgac ggactcacgt gctgctccgt ccccatgagc tcagtggacc tgtctatgta 300 gagcagtcag acagtgcctg ggatagagtg agagttcagc cagtaaatcc aagtgattgt 360 catteetgte tgcattagta acteccaace tagatgtgaa aacttagtte tttetcatag 420 gttgctctgc ccatggtccc actgcagacc caggcactct ccggaagcct ggaaatcacc 480 cgtgtcttct gcctgctccc gctcacatcc cacacttgtg ttcagtcact gagttacaga 540 ttttgcctcc tcaatttctc ttgtcttagt cccatcctct gttcccctgg ccagtttgtc 555 tagctgtgtg gtctc
- <210> 38
- <211> 19
- <212> DNA
- <213> Artificial Sequence

WO 99/31236 -20 - PCT/IB98/02122

<220> <223>	01 io	onu	clec	tide	<u> </u>											
	V119	,0110	.0100													
<400>																19
ggcca	tacac	: ככ	gagt	gac												13
<210>	3 9															
<211>																
<212>																
<213>	Arti	fic	ial	Sequ	ience	=										
<220>																
<223>	Olig	onu	clec	cid	e											
-4005	20															
<400> atata		ac	gcac	acc												19
	J		_													
<210>	40															
<211>	568															
<212>																
<213>	HOMO	Se	pre	15												
<220>																
<221>																
<222>	74	71														
<221>	sig_	per	tide	9												
<222>													,			
<223>	Von scor		-	mat	rix											
				ALSL	LLA/	LL										
<221> <222>		_	_	al												
~~~	337.		14													
<221>																
<222>	554	5	58													
<400>	40															
gggac	c ato	g ti	tc a	cc a	gc a	.cc g	gc t	cc a	igt g	igg c	tc t	ac a	ag g	icg c	ct	4 8
	Met			hr S	er T	hr G		er S -25	Ser C	ly I	Jeu 1	yr L	ys A 20	Ma F	ro	
ctg t	cor a	aci i	30 agc	ctt	ctq	ctg			agt	gcc	ctc			ctg	ctc	96
Leu S	er Ly	ys :	Ser	Leu	Leu	Leu	Val	Pro	Ser	Ala	Leu	Ser	Leu	Leu	Leu	
		15					-10				ara	-5	GaC.	ctt	cac	144
gcc c Ala L	CC CI	בר בוו	ctg Leu	Pro	His	Cvs	Gln	Lvs	Pro	Phe	Val	Tyr	Asp	Leu	His	
1					5					10					15	
gca g	tc a	ag	aac	gac	ttc	cag	att	tgg	agg	ttg	ata	tgt	gga	aga	ata	193
Ala V	al L	ys .	Asn		Phe	Gln	Ile	Trp	Arg 25	Leu	Ile	Cya	GIY	Arg	TIE	
att t	ימר כי		gat	20 tta	aaa	σat	act	ttc		aqt	agt	ctg	ctt		tat	24
Ile C	ys L	eu	Asp	Leu	Lys	Asp	Thr	Phe	Cys	Ser	Ser	Leu	Leu	Ile	Tyr	
			35					40					45			28
aat t Asn F	tt a	<b>99</b>	ata	Dha	gaa	aga	aga	Tvr	gga	ser	aga Ara	Lvs	Phe	Ala	Ser	20
Wall P	ne a		***	- 116	GIG	y	55	1 -	1		3	60				

WO 99/31236 -21- PCT/IB98/02122

ttt ttg ctg ggt acc tgg gtt ttg tca gcc tta ttt gac ttt ctc ctc  Phe Leu Leu Gly Thr Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu  65 70 75	336										
att gaa gct atg cag tat ttc ttt ggc atc act gca gct agt aat ttg Ile Glu Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu 80 85 90 95	384										
CCT tct gga tta atc ttt tgt tgt gct ttt tgc tct gag act aaa ctc Pro Ser Gly Leu Ile Phe Cys Cys Ala Phe Cys Ser Glu Thr Lys Leu 100 105 110	432										
ttc tta tca aga caa gct atg gca gag aac ttt tcc atc taataaattt Phe Leu Ser Arg Gln Ala Met Ala Glu Asn Phe Ser Ile 115 120	481										
aagagtagat tcatctgtat ggttgagagt aggctctgac tatgtatatg tgtataataa											
acctacatat ccaaaaaaaa aaaaaaa											
<210> 41											
<211> 569 <212> DNA											
<213> Homo sapiens											
<220>											
<221> CDS											
<222> 168332											
<221> polyA_signal											
<222> 557562											
<400> 41											
agggggggtg gggceatggt ggtcttgcgg gcggggaaga agacctttct ccccctctc	60 120										
tgccgcgcct tcgcctgccg cggctgtcaa ctcgctccgg agcgcggcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac											
tgccgcgcct tcgcctgccg cggctgtcaa ctcgctccgg agcgcggcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp	120										
tgccgcgcct tcgcctgccg cggctgtcaa ctcgctccgg agcgcggcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp  1 ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat	120										
tgccgcgcct tcgcctgccg cggctgtcaa ctcgctccgg agcgcggcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp  1 ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr	120 176										
tgccgcgcct tcgcctgccg cggctgtcaa ctcgctccgg agcgcggcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp  1 ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr  5 10 15 aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga	120 176										
tgccgcgcct tcgcctgccg cggctgtcaa ctcgctccgg agcggcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat  Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr  5  10  15  aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga  Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly	120 176 224										
tgccgcgct tcgcctgccg cggctgtcaa ctcgctccgg agcggcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp 1  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr 5 10 15  aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly 20 25 30 35	120 176 224										
tgccgcgct tcgcctgccg cggctgtcaa ctcgctccgg agccgcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp 1  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr 5 10 15  aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly 20 25 30 35  aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa aag Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys	120 176 224 272										
tgccgcgct tcgcctgccg cggctgtcaa ctcgctccgg agccgcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp 1  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr 5 10 15  aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly 20 25 30 35  aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa aag Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys 61n Lys 61	120 176 224 272										
tgccgcgct tcgcctgccg cggctgtcaa ctcgctccgg agccgcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp 1  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr 5 10 15  aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly 20 25 30 35  aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa aag Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys 40 45 50  aag agg agc aac taggagtcca ctctgaccca gccagagtcc aggtttccac Lys Arg Ser Asn	120 176 224 272 320										
tgccgcgct tcgcctgccg cggctgtcaa ctcgctccgg agccgcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac  Met Ala Asp  1  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr  5 10 15  aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly 20 25 30 35  aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa aag Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys  40 45 50  aag agg agc aac taggagtcca ctctgaccca gccagagtcc aggtttccac Lys Arg Ser Asn  55	120 176 224 272 320										
tgccgcgct tcgcctgccg cggctgtcaa ctcgctccgg agccgcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac  Met Ala Asp  1  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr  5 10 15  aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly 20 25 30 35  aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa aag Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys  40 45 50  aag agg agc aac taggagtcca ctctgaccca gccagagtcc aggtttccac Lys Arg Ser Asn  55  aggaagcaga tggagctcct ttcacagggg ctctgagaaa aactggagcc gatctcaaga agccccacat cttcctaagg ggccccatgg cctgtttggg ggcagggtag gtcctggggc	120 176 224 272 320 372 432 492										
tgccgcgct tcgcctgccg cggctgtcaa ctcgctccgg agccgcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac  Met Ala Asp  1  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr  5 10 15  aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly 20 25 30 35  aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa aag Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys  40 45 50  aag agg agc aac taggagtcca ctctgaccca gccagagtcc aggtttccac Lys Arg Ser Asn  55	120 176 224 272 320 372 432 492 552										
tgccgcgct tcgcctgccg cggctgtcaa ctcgctccgg agccgcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac  Met Ala Asp  1  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr  5 10 15  aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly 20 25 30 35  aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa aag Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys  40 45 50  aag agg agc aac taggagtcca ctctgaccca gccagagtcc aggtttccac Lys Arg Ser Asn  55  aggaagcaga tggagctcct ttcacagggg ctctgagaaa aactggagcc gatctcaaga agccccacat cttcctaagg ggccccatgg cctgtttggg ggcagggtag gtcctggggc	120 176 224 272 320 372 432 492										
tgccgcgct tcgcctgccg cggctgtcaa ctcgctccgg agccgcgc cgagcgcagg gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac  Met Ala Asp  Met Ala Asp  1  ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr  5	120 176 224 272 320 372 432 492 552										

<210> 42 <211> 895 <212> DNA <213> Homo sapiens <220> <221> CDS

<222> 51..251

WO 99/31236 -22 - PCT/IB98/02122

```
<221> sig_peptide
<222> 51..110
<223> Von Heijne matrix
      score 5.3
      seq ALIFGGFISLIGA/AF
<221> polyA_signal
<222> 849..854
<221> polyA site
<222> 882..895
<400> 42
ccgagagtgc cgggcggtcg gcgggtcagg gcagcccggg gcctgacgcc atg tcc
                                                                    56
                                                      Met Ser
egg aac etg ege ace geg ete att tte gge gge tte ate tee etg ate
Arg Asn Leu Arg Thr Ala Leu Ile Phe Gly Gly Phe Ile Ser Leu Ile
            -15
                               -10
                                                   - 5
ggc gcc gcc ttc tat ccc atc tac ttc egg ccc cta atg aga ttg gag
                                                                   152
Gly Ala Ala Phe Tyr Pro Ile Tyr Phe Arg Pro Leu Met Arg Leu Glu
                                           10
gag tac aag aag gaa caa gct ata aat cgg gct gga att gtt caa gag
                                                                   200
Glu Tyr Lys Lys Glu Gln Ala Ile Asn Arg Ala Gly Ile Val Gln Glu
15
                   20
                                       25
gat gtg cag cca cca ggg tta aaa gtg tgg tct gat cca ttt ggc agg
                                                                   248
Asp Val Gln Pro Pro Gly Leu Lys Val Trp Ser Asp Pro Phe Gly Arg
                                   40
aaa tgagaggct gtcatcagct ctgattaaga aaggagattt cttcatgctt
                                                                    301
Lys
tcgattctgc atggggtaca gccagtcacc tcaccagaga atgacggctg gagaagaaaa
                                                                   361
ctctgtaata ccataaataa gagtgcttgt aataaaagac tgtgcacaag gattaatatt
                                                                    421
tcccttctta agtatcaaaa gaactctgga acaaattata ccattaggaa ggttttcatg
                                                                    481
attcagttga ttttccaaaa atgaagctat ctcacccagc tgggtttgga ggagcaatct
                                                                    541
gcttattatt ctgtcgttac cacttactca agcgagctgt gatatgaata caagcaacca
                                                                    601
                                                                    661
gtgggctcgg gaaggtccgg gtctcttctg ccatcttcca gataagagat ttcagtaaaa
                                                                   721
aactgccatg ctgagctgcc ttatagagct cttcgaaaat gttcgagttg ataaagctct
ttgaggacaa ggtacttcgt gcacctcatg ctgaagattg caccatgttg gaagataaat
                                                                    781
atgaagcaag tcaaactaga tgcatacact tgtgtagaaa tcaataatca attaatagaa
                                                                    841
895
<210> 43
<211> 691
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 20..613
<221> sig_peptide
<222> 20..82
<223> Von Heijne matrix
      score 10
      seq LWALAMVTRPASA/AP
<400> 43
```

atacettaga ceetcagte atg eca gtg eet get etg tge etg etc tgg gee

Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala

						-20	)				-15	5				
ctg Leu -10	gca Ala	atg Met	gtg Val	acc Thr	cgg Arg	cct Pro	gcc Ala	tca Ser	gcg Ala	gcc Ala 1	ccc Pro	atg Met	ggc	ggc Gly 5	cca Pro	100
gaa					gag Glu											148
					ctc Leu											196
					aac Asn											244
	_		_		gtc Val 60	-		-		-	_	_	-	_		292
cgg	gca Ala	agc Ser	ctg	ttg Leu 75	gag Glu	act Thr	cag Gln	atg Met	gag Glu 80	gag Glu	gat Asp	att Ile	ctg Leu	cag Gln 85	ctg Leu	340
					gct Ala									Ala		388
aag Lys	gtg Val	cta Leu 105	cgg Arg	gac Asp	agc Ser	gtg Val	cag Gln 110	cgg Arg	cta Leu	gaa Glu	gtc Val	cag Gln 115	ctg Leu	agg Arg	agc Ser	436
gcc Ala	tgg Trp 120	ctg Leu	ggc Gly	cct Pro	gcc Ala	tac Tyr 125	cga Arg	gaa Glu	ttt Phe	gag Glu	gtc Val 130	Leu	aag Lys	gct Ala	cac His	484
gct Ala 135	gac	aag Lys	cag Gln	agc Ser	cac His 140	atc Ile	cta Leu	tgg Trp	gcc Ala	ctc Leu 145	Thr	ggc Gly	cac His	gtg Val	cag Gln 150	532
cgg	cag Gln	agg Arg	cgg Arg	gag Glu 155	atg Met	gtg Val	gca Ala	cag Gln	cag Gln 160	cat	cgg	ctg Leu	cga Arg	cag Gln 165	Ile	580
			Leu	cac His	aca Thr				cca			atct	gcc		tggaac	633
170 175 tgaggaccaa tcatgctgca aggaacactt ccacgccccg tgaggcccct gtgcaggg												aggg	691			

<210> 44

<211> 458

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 12..416

<221> sig_peptide

<222> 12..86

<223> Von Heijne matrix score 4 seq LVVMVPLVGLIHL/GW

<221> polyA_signal

<222> 425..430

<221> polyA_site <222> 445..458

<400> 44 gctgaagtac t atg agc ctt cgg aac ttg tgg aga gac tac aaa gtt ttg Met Ser Leu Arg Asn Leu Trp Arg Asp Tyr Lys Val Leu	50										
-25 -20 -15  gtt gtt atg gtc cct tta gtt ggg ctc ata cat ttg ggg tgg tac aga  Val Val Met Val Pro Leu Val Gly Leu Ile His Leu Gly Trp Tyr Arg  -10 -5 1	98										
atc aaa agc agc cct gtt ttc caa ata cct aaa aac gac gac att cct  Ile Lys Ser Ser Pro Val Phe Gln Ile Pro Lys Asn Asp Asp Ile Pro  10 15 20	146										
gag caa gat agt ctg gga ctt tca aat ctt cag aag agc caa atc cag Glu Gln Asp Ser Leu Gly Leu Ser Asn Leu Gln Lys Ser Gln Ile Gln 25 30 35	194										
ggg aag nta gca ggc ttg caa tct tca ggt aaa gaa gca gct ttg aat Gly Lys Xaa Ala Gly Leu Gln Ser Ser Gly Lys Glu Ala Ala Leu Asn 40 45 50	242										
ctg agc ttc ata tcg aaa gaa gag atg aaa aat acc agt tgg att aga Leu Ser Phe Ile Ser Lys Glu Glu Met Lys Asn Thr Ser Trp Tle Arg 55 60 65	290										
aag aac tgg ctt ctt gta gct ggg ata tct ttc ata ggt gac cat ctt Lys Asn Trp Leu Leu Val Ala Gly Ile Ser Phe Ile Gly Asp His Leu 70 75 80	338										
gga aca tac ttt ttg cag agg tct gca aag cag tct gta aaa ttt cag Gly Thr Tyr Phe Leu Gln Arg Ser Ala Lys Gln Ser Val Lys Phe Gln 85 90 95 100	386										
tct caa agc aaa caa aag agt att gaa gag tgaagtaaaa taaatatttg Ser Gln Ser Lys Gln Lys Ser Ile Glu Glu 105 110	436										
gaattactaa aaaaaaaaaa aa	458										
<pre>&lt;210&gt; 45 &lt;211&gt; 2036 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 2761040 </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 276485 </pre> <pre>&lt;223&gt; Von Heijne matrix</pre>											
equipment of the control of the cont	60 120 180 240 293										
Cag ttt agg gag tgg ttt ttg aaa gag ttt cct caa atc aga tgg aag Gln Phe Arg Glu Trp Phe Leu Lys Glu Phe Pro Gln Ile Arg Trp Lys -60 -55 -50	341										
att cag gag tee ata gaa agg ett egt gte att gea aat gag att gaa	389										

WO 99/31236 -25- PCT/IB98/02122

Ile	Gln	Glu	Ser	Ile	Glu	Arg	Leu	Arg	Val	Ile	Ala	Asn	Glu -35	Ile	Glu	
aaq	gtc	cac	aga	qqc	tgc	gtc	atc	gcc	aat	gtg	gtg	tct	ggc	tcc.	act	437
Lvs	Val	His	Ara	Glv	Cvs	Val	Ile	Ala	Asn	Val	Val	Ser	Gly	Ser	Thr	
•		-30	J	4	•		-25					-20	•			
ggc	atc	ctq	tct	gtc	att	ggc	gtt	atg	ttg	gca	cca	ttt	aca	gca	ggg	485
Gly	Ile	Leu	Ser	Val	Ile	Gly	Val	Met	Leu	Ala	Pro	Phe	Thr	Ala	Gly	
•	-15					-10					- 5				•	
ctg	agc	ctg	agc	att	act	gca	gct	999	gta	ggg	ctg	gga	ata	gca	tct	533
Leu	Ser	Leu	Ser	Ile	Thr	Ala	Āla	Gly	Val	Gly	Leu	Gly	Ile	Ala	Ser	
1				5	,				10					15		
gcc	acg	gct	999	atc	gcc	tcc	agc	atc	gtg	gag	aac	aca	tac	aca	agg	581
Ala	Thr	Ala	Gly	Ile	Ala	Ser	Ser	Ile	Val	Glu	Asn	Thr	Tyr	Thr	Arg	
			20					25					30			
	gca															629
Ser	Ala	Glu	Leu	Thr	Ala	Ser	Arg	Leu	Thr	Ala	Thr		Thr	Asp	Gln	
		35					40					45				
ttg	gag	gca	tta	agg	gaç	att	ctg	cat	gac	atc	aca	CCC	aat	gtg	ctt	677
Leu	Glu	Ala	Leu	Arg	Asp		Leu	His	Asp	Ile		Pro	Asn	Val	Leu	
	50					55					60					725
tcc	ttt	gca	ctt	gat	ttt	gac	gaa	gcc	aca	aaa	atg	att	gcg	aat	gat	725
	Phe	Ala	Ļeu	Asp		Asp	GIU	ALA	Thr		mec	ile	Ala	ASI	Asp 80	
65					70					75	~~~			++~		773
gtc	cat His	aca	CEC	agg	aga	505	aaa	312	Th-	y.t	Gly	Ava	Dro	Len	Tle	,,,
val	HIS	inr	rea	85	Arg	261	гλя	WIG	90	val	Gry	Αrg	FIU	95	110	
aa+	tgg	~~~			cct	2+2	225	att		aaa	aca	cta	апа		cat	821
Ala	Trp	Ara	Tur	Wal	Dro	Tla	Aen	Val	Val	Glu	Thr	Len	Ara	Thr	Ara	
AIG	пр	Arg	100	Val	PIO,	110	7311	105	141	014	• • • •		110		5	
aaa	gcc	ccc		caa	ata	ata	aca		ota	acc	caa	aac		aac	ааσ	869
999	Ala	Pro	Thr	723	Tle	Val	Ara	Lvs	Val	Ala	Ara	Asn	Leu	Glv	Lvs	
		115	•	3			120	-,-		•	5	125		•	•	
acc	act		aat	atc	ctc	att		ctq	qat	gta	gtc	aac	ctt	gtg	caa	917
Ala	Thr	Ser	Gly	Val	Leu	Val	Val	Leu	Asp	Val	Val	Asn	Leu	Val	Gln	
	130		•			135			_		140					
gac	tca	ctg	gac	ttg	cac	aag	999	gaa	aaa	tcc	gag	tct	gct	gag	ttg	965
Asp	Ser	Leu	Asp	Leu	His	Lys	Gly	Glu	Lys	Ser	Glu	Ser	Ala	Glu	Leu	
145					150					155					160	_
ctg	agg	cag	tgg	gct	cag	gag	ctg	gag	gag	aat	ctc	aat	gag	ctc	acc	1013
Leu	Arg	Gln	Trp	Ala	Gln	Glu	Leu	Glu	Glu	Asn	Leu	Asn	Glu			
				165					170					175		
cat	atc	cat	cag	agt	cta	aaa	gca	ggc	tag	gccc	aat	tgtt	gcgg	ga		1060
His	Ile	His	Gln	Ser	Leu	Lys	Ala	_								
			180				_	185								1120
agt	cagg	gac	ccca	aacg	ga g	ggac	tggc	t ga	agcc	atgg	Cag	aaga	acg	cgga	ttgtga	1180
aga	ECC.	atg	gaca	ttta	tt a	gttc	ccca	aac	caat	tact		caat		cact	geetgt	1240
CEE	Cacc	gca	atct	ctaa	ac a	caaa	cege	y ad	ttac	ttat	990	tect	.cat	cctc	tececa	1300
atc	aata	ccc	ttgt	gatt		cacy	cert		.ccac	++~		-2261	.aac	caaa	tcagct ttgtag	1360
gag	gagg	gtg	cacg	ccac	25 2	ayya -aaa	atet	9 0	icaca	tta	. 900	2202	aca	ggat	aacago	1420
ago	acgt	gra	~~~	aaca	a	cyaa	acct	·	acto	tase	cas	cagt	aaa	2200	aacagc gtggag	1480
aat	cgtt	cay	9994	taay	ay a	tess	3270		tacco	egac	ata	tra	rtga	atto	ttttc	1540
rag	ayuc	aca aa=	2025		72 T	2222	2022	it or	335	cta		itaa	itct	ata	atggcc	1600
Fac	++~~	33ª	toon	cato	94 Y	+2+	iates	1a (7:	ctat	aggr	- JJ:	TAAR	caaa	CCC	cagtete	1660
	tant	ac+	-336	aact		tace	IAACE	10 0:	aaatt	322	, ~C	caat	aaat	ttt	gtcaga	1720
	atta	ctc	tcaa	3300	ict c	toto	ctas	t as	agato	ttat	, ca	atga	caat	gate	gcctgaa	1780
200	オーレザ	tan	caat	+++=	at t	tet	2000	a to	chai	aat	cto	gtaa	tctc	acc	ctgcctc	1840
car	ttac	ctt	atas	tatt	ct =	ttac	ctte	it a	aagta	agata	at	cttt	qtqa	ccc	acaccct	1900
art	cara	CAC	2000	tecc	ct t	ttac	aaat		ctaal	taaa	aac	ttac	tgat	ttt	gcagctt	1960
ate	agan	atc	acqq	aacc	ta	taat	atat	g at	tgtc	tccc	c ta	gaca	ccta	gct	ttaaaat	2020
	aaaa					J		-								2036

```
<210> 46
<211> 1276
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 443..619
<221> sig_peptide
<222> 443..589
<223> Von Heijne matrix
      score 7
      seq LICVVCLYIVCRC/GS
<221> polyA_site
<222> 1267..1276
<400> 46
gaggcactca cggcatttca ttgctacttt aattttcatt attatgggat tgattgctgt
cacagetact getgeagtag etggagttge tttgeattee acagtacaaa cageagacta
                                                                      120
tgtaaataat tggtagaaaa attctactct gctgtggaat taccaagata atatagacca
                                                                      180
                                                                      240
gaaactagct gatcaaatta atgatctcca acaaactgta atgtggctag gggatcatat
agttagttta gaatatagaa tgcggttaca atgtgattga aatacctctg atttttgcat
                                                                      360
tactcctcat ctgtgtaatg aaacagagca tgagtgggaa aaagttaaga gatatttaaa
aggtcatact agaaatttat ctttggatat tgcaaagcta aaggaacaag tatttcaagc
                                                                      420
ccctcagata catctgacac ta atg cca gga act gaa gtg ctt gaa gga gct
                                                                      472
                         Met Pro Gly Thr Glu Val Leu Glu Gly Ala
                                          -45
                                                                      520
aca gac gga tta gca gct att aac ctg cta aaa tgg atc aag aca ctt
Thr Asp Gly Leu Ala Ala Ile Asn Leu Leu Lys Trp Ile Lys Thr Leu
                                     -30
                - 35
gga ggc tot gtg att toa atg att gtg ott tta atc tgt gtt gtt tgt
                                                                      568
Gly Gly Ser Val Ile Ser Met Ile Val Leu Leu Ile Cys Val Val Cys
                                 -15
                                                                      616
ctt tat ata gtc tgt aga tgc gga agc cac ctc tgg aga gaa agc cac
Leu Tyr Ile Val Cys Arg Cys Gly Ser His Leu Trp Arg Glu Ser His
                                                                      669
cac tgagagcaag caatgatagc tgtggcggtt ttgcaaaaag aaaagggaga
His
10
                                                                       729
caagegeeca getatagtta ecaataaage atggtaetgg tattaaaata ggeatgtgtt
                                                                       789
ctgttccaat ggaacagaat agagaaccca gaaacaaagc caaatattta cagccaactg
                                                                       849
atctctgaca aagcaaacaa aaacataaag tggggaaagg acaccctatt ccacaaatag
tgcagggata attggcaagc cacatgtaga aaaatgaagc tggatcctcg tctctcactt
                                                                       909
tatacaaaaa tcaactcaaa atgggtcaaa gtcttaactc taagacctga aaccataaca
                                                                       969
                                                                      1029
attoragana ataacattgg anaanactott ctagacattg gtttaggcan anagttcatg
                                                                      1089
accaagaacc caaaagcaaa tgcaataaaa aggaagataa atagatggga cctaattaag
                                                                      1149
ctgaaaagct tctgcatagc aaaaggaata atcagcagag caaacagaca acccacaggg
                                                                      1209
tgggagaaaa tatttgcaag ctatgtatct gacaatggac taatatccag aatctacaag
gaattcaaac aattagcaag aaaaaacact tgtattgtgt ttgctctgta aatcagcaaa
                                                                      1269
                                                                      1276
```

<211> 747

<212> DNA

<213> Homo sapiens

```
<221> CDS
<222> 206..745
accagaagca ggtgatttcc gagctcagca atgctcagct cataatgatg tcaagcacca
                                                                     60
                                                                     120
tggccagttt tatgaatggc ttcctgtgtc taatgaccct gacaacccat gttcactcaa
                                                                     180
gtgccaagcc aaaggaacaa ccctggttgt tgaactagca cctaaggtct tagatggtac
gcgttgctat acagaatctt tggat atg tgc atc agt ggt tta tgc caa att
                                                                     232
                            Met Cys Ile Ser Gly Leu Cys Gln Ile
gtt ggc tgc gat cac cag ctg gga agc acc gtc aag gaa gat aac tgt
                                                                     280
Val Gly Cys Asp His Gln Leu Gly Ser Thr Val Lys Glu Asp Asn Cys
                                        20
10
                    15
ggg gtc tgc aac gga gat ggg tcc acc tgc cgg ctg gtc cga ggg cag
                                                                     328
Gly Val Cys Asn Gly Asp Gly Ser Thr Cys Arg Leu Val Arg Gly Gln
                                    35
                                                       40
                                                                     376
tat aaa too dag oto too goa aco aaa tog gat gat act gtg gtt goa
Tyr Lys Ser Gln Leu Ser Ala Thr Lys Ser Asp Asp Thr Val Val Ala
           45
                                50
att ccc tat gga agt aga cat att cgc ctt gtc tta aaa ggt cct gat
                                                                     424
Ile Pro Tyr Gly Ser Arg His Ile Arg Leu Val Leu Lys Gly Pro Asp
                           65
                                                70
                                                                      472
cac tta tat ctg gaa acc aaa acc ctc cag ggg act aaa ggt gaa aac
His Leu Tyr Leu Glu Thr Lys Thr Leu Gln Gly Thr Lys Gly Glu Asn
                       80
agt etc age tec aca gga act tte ett gtg gae aat tet agt gtg gae
                                                                      520
Ser Leu Ser Ser Thr Gly Thr Phe Leu Val Asp Asn Ser Ser Val Asp
                    95
                                        100
                                                                      568
ttc cag aaa ttt cca gac aaa gag ata ctg aga atg gct gga cca ctc
Phe Gln Lys Phe Pro Asp Lys Glu Ile Leu Arg Met Ala Gly Pro Leu
                                    115
                110
aca gca gat ttc att gtc aag att cgt aac tcg ggc tcc gct gac agt
                                                                      616
Thr Ala Asp Phe Ile Val Lys Ile Arg Asn Ser Gly Ser Ala Asp Ser
                                130
                                                    135
            125
                                                                      664
aca gtc cag ttc atc ttc tat caa ccc atc atc cac cga tgg agg gag
Thr Val Gln Phe Ile Phe Tyr Gln Pro Ile Ile His Arg Trp Arg Glu
                            145
acg gat tto ttt cot tgc tca gca acc tgt gga gga ggt tat cag ctg
                                                                      712
Thr Asp Phe Phe Pro Cys Ser Ala Thr Cys Gly Gly Tyr Gln Leu
                        160
                                                                      747
aca tog got gag tgo tac gat otg agg ago aac og
Thr Ser Ala Glu Cys Tyr Asp Leu Arg Ser Asn
                    175
```

<220>

<211> 561

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 36..521

<221> sig_peptide

<222> 36..104

<223> Von Heijne matrix score 7.4 seq VLLLAALPPVLLP/GA

<221> polyA_signal <222> 528..533 <221> polyA_site <222> 548..561 <400> 48 gacgeetett teageeeggg ategeeecag eaggg atg gge gae aag ate tgg Met Gly Asp Lys Ile Trp 101 Leu Pro Phe Pro Val Leu Leu Leu Ala Ala Leu Pro Pro Val Leu Leu -10 cct 999 gcg gcc ggc ttc aca cct tcc ctc gat agc gac ttc acc ttt 149 Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu Asp Ser Asp Phe Thr Phe 10 197 acc ctt ccc gcc ggc cag aag gag tgc ttc tac cag ccc atg ccc ctg Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe Tyr Gln Pro Met Pro Leu 25 20 aag gcc tcg ctg gag atc gag tac caa gtt tta gat gga gca gga tta 245 Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val Leu Asp Gly Ala Gly Leu 45 40 35 293 gat att gat ttc cat ctt gcc tct cca gaa ggc aaa acc tta gtt ttt Asp Ile Asp Phe His Leu Ala Ser Pro Glu Gly Lys Thr Leu Val Phe 55 gaa caa aga aaa tca gat gga gtt cac act gta gag act gaa gtt ggt 341 Glu Gln Arg Lys Ser Asp Gly Val His Thr Val Glu Thr Glu Val Gly 70 gat tac atg ttc tgc ttt gac aat aca ttc agc acc att tct gag aag 389 Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe Ser Thr Ile Ser Glu Lys 90 85 437 gtg att ttc ttt gaa tta atc ccg gat aat atg gga gaa cag gca caa Val Ile Phe Phe Glu Leu Ile Pro Asp Asn Met Gly Glu Gln Ala Gln 105 100 485 gaa caa gaa gat tgg aag aaa tat att act ggc aca gat ata ttg gat Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr Gly Thr Asp Ile Leu Asp 120 115 atg aaa ctg gaa gac atc ctg gtc agt atg gtc ttc taataaaata 531 Met Lys Leu Glu Asp Ile Leu Val Ser Met Val Phe 135 561 aaaattatta acagccaaaa aaaaaaaaaa

<210> 49

<211> 632

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 36..395

<221> sig_peptide

<222> 36..104

<223> Von Heijne matrix score 7.4 seq VLLLAALPPVLLP/GA

<221> polyA_signal

<222> 599..604

	l> po 2> 63		site	2												
< 4 2 2	4> 6.	.9	32													
	> 49											· · ·			~~	<b>5</b> 3
gac	gcct	ett t	cago	ccgg	gg at	cgco	ccaç	, caç				Asp 1	Lys 1	ile T		53
ct <b>a</b>	CCC	FFC		gtg	ctc	ctt	cta	acc	act	cta	cat		-20 ata	cta	cta	101
				Val												
		-15					-10					- 5				
cct	999	gcg	gcc	ggc Gly	ttc	aca	CCE	tcc	CtC	gat	agc	gac	Dhe	acc	Phe	149
PFO	GIY	HIG	Ala	GIY	5	IIIL	FIO	361	Deu	10	361	ABP	FIIC	1,111	15	
acc	ctt	ccc	gcc	ggc	cag	aag	gag	tgc	ttc	tac	cag	ccc	atg	ccc	ctg	197
Thr	Leu	Pro	Ala	Gly	Gln	Lys	Glu	Cys		Tyr	Gln	Pro	Met		Leu	
220	000	+ ca	cta	20 gag	atc	gag	tac	caa	25 att	tta	gat	gga	αca	30 gga	tta	245
Lys	Ala	Ser	Leu	Glu	Ile	Glu	Ţyr	Gln	Val	Leu	Asp	Gly	Ala	Gly	Leu	
-			35					40					45			
gat	att	gat	ttc	cat	ctt	gcc	tct	cca	gaa	ggc	aaa	acc	tta	gtt	ttt	293
qeA	He	Asp 50	Pne	His	Leu	Ala	ser 55	Pro	GIU	GIY	гÀг	60	Leu	Vai	PILE	
qaa	caa		aaa	tca	gat	gga		cac	acg	tgt	ata		agt	aaa	aat	341
Glu	Gln	Arg	Lys	Ser	Asp	Gly	Val	His	Thr	Сув	Ile	Arg	Ser	Lys	Asn	
	65					70			<b>-</b>		75					389
999	cca	ggc	act Th~	gcg Ala	gtt	cac	gcc	Tyr	Agn	Pro	Ser	Thr	Phe	Ara	Glv	303
80	PIO	GIY	1111	AIG	85	1123	ALU	-1-	7.0	90	-				95	
	gtg	taga	agac	tga (	agtt	ggtg	at t	acat	gttc	t gci	tttg	acaa	tac	attc	agc	445
	Val															505
acc	attt	etg (	agaa	ggtg	at t	ttct	ttga	a tt	aatc taac	ctgg	ata	atat tatt	999	tato	caggca aaactg	505 565
caag	ggac	aag	aaga raar	cagt.	aa g at o	adat.	acac tcta	a ta	cggc aaat	acag	att	atta	aca	qcca	aaaaaa	625
	aaaa		-33-	0450		3								•		632
															•	
-21	0 > 5	n														
	1> 3															
<21	2 > D	NA														
<21	3 > H	omo	sapi	ens												
<22	0.															
	1> C	DS														
<22	2> 2	14	1													
	1> p 2> 3		_sig	naı												
122		20	333													
			_sit	e.												
<22	2 > 3	57	370													
- 40	0 > 5	^														
Cta	ggac	ttc	taac	ctca	ica a	ata d	itt o	aq a	atg a	act c	igg (	gtg	tagc	agtg	cc	51
3	2246		- 33			det \	/al (	slu i	1et '	Thr C	Sly	Val	•	_ •		
						1				5						111
aag	tcga	ggc	tgt	aaaq	gc (	cttc	cacct	t to	actc	cgt	g ct	cgtg	ccct	CCC	ccattgt	171
tag	gaga	agg	gcat	gcto	ag 9	ccaa	cca	ac c	aaaa	ctate	- 99 : ct	gaat	tage	aac	cacacgg cctgaca	231
cat	ataa	aca	agto	caac	egg (	acac	cggaa	ag a	tcca	cctag	g tc	aago	ccaa	cca	agactgg	291
cag	agct	gcc	aag	ctgad	cca	ctta	aggc	gc a	tgag	gaat	a aa	cact	cgtt	gct	gcatgcc	351
_	-			aaaa												370

```
<210> 51
<211> 994
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 35..631
<221> sig_peptide
<222> 35..160
<223> Von Heijne matrix
      score 8.6
      seg ASLFLLLSLTVFS/IV
<221> polyA_signal
<222> 901..906
<221> polyA_site
<222> 979..994
<400> 51
ataattggag ctgcaaagca gatcgtgaca agag atg gac ggt cag aag aaa aat
                                      Met Asp Gly Gln Lys Lys Asn
tgg aag gac aag gtt gtt gac ctc ctg tac tgg aga gac att aag aag
                                                                     103
Trp Lys Asp Lys Val Val Asp Leu Leu Tyr Trp Arg Asp Ile Lys Lys
                                                            -20
                    -30
                                        -25
-35
act gga gtg gtg ttt ggt gcc agc cta ttc ctg ctg ctt tca ttg aca
                                                                      151
Thr Gly Val Val Phe Gly Ala Ser Leu Phe Leu Leu Ser Leu Thr
                -15
                                    -10
gta ttc age att gtg age gta aca gcc tac att gcc ttg gcc ctg ctc
                                                                      199
Val Phe Ser Ile Val Ser Val Thr Ala Tyr Ile Ala Leu Ala Leu Leu
                          . 5
           1
tet gtg acc atc age ttt agg ata tac aag ggt gtg atc caa gct atc
                                                                      247
Ser Val Thr Ile Ser Phe Arg Ile Tyr Lys Gly Val Ile Gln Ala Ile
                        20
cag aaa tca gat gaa ggc cac cca ttc agg gca tat ctg gaa tct gaa
                                                                      295
Gln Lys Ser Asp Glu Gly His Pro Phe Arg Ala Tyr Leu Glu Ser Glu
                                         40
30
                    35
                                                                      343
gtt gct ata tct gag gag ttg gtt cag aag tac agt aat tct gct ctt
Val Ala Ile Ser Glu Glu Leu Val Gln Lys Tyr Ser Asn Ser Ala Leu
                                     55
                50
                                                                      391
ggt cat gtg aac tgc acg ata aag gaa ctc agg cgc ctc ttc tta gtt
Gly His Val Asn Cys Thr Ile Lys Glu Leu Arg Arg Leu Phe Leu Val
                                 70
            65
                                                                      439
gat gat tta gtt gat tot ctg aag ttt gca gtg ttg atg tgg gta ttt
Asp Asp Leu Val Asp Ser Leu Lys Phe Ala Val Leu Met Trp Val Phe
                                                 90
                             85
                                                                      487
acc tat gtt ggt gcc ttg ttt aat ggt ctg aca cta ctg att ttg gct
Thr Tyr Val Gly Ala Leu Phe Asn Gly Leu Thr Leu Leu Ile Leu Ala
                                             105
    95
                         100
                                                                      535
ctc att tca ctc ttc agt gtt cct gtt att tat gaa cgg cat cag gca
Leu Ile Ser Leu Phe Ser Val Pro Val Ile Tyr Glu Arg His Gln Ala
                    115
                                         120
                                                                       583
cag ata gat cat tat cta gta ctt gca aat aag aat gtt aaa gat gct
Gln Ile Asp His Tyr Leu Val Leu Ala Asn Lys Asn Val Lys Asp Ala
                                     135
                 130
atg gct aaa atc caa gca aaa atc cct gga ttg aag cgc aaa gct gaa
                                                                       631
```

Met Ala Lys Ile Gln Ala Lys Ile Pro Gly Leu Lys Arg Lys Ala Glu  145  150  155  tgaaaacgcc caaaataatt agtaggagtt catctttaaa ggggatattc atttgattat acgggggagg gtcagggaga aacgaacctt gacgttgcag tgcagtttca cagatcgttg ttagatcttt atttttagcc atgcactgtt gtgaggaaaa attacctgtc ttgactgcca tgtgttcatc atcttaagta ttgtaagctg ctatgtatgg atttaaaccg taatcatatc tttttcctat ctatctgagg cactggtgga ataaaaaaacc tgtatatttt actttgttgc agatagtctt gccgcatctt ggcaagttgc agagatggtg gagctagaaa aaaaaaaaac aaa	691 751 811 871 931 991
<210> 52 <211> 412 <212> DNA ^M <213> Homo sapiens	
<220> <221> CDS <222> 271399	
<400> 52 geogetageg cetegagega tgeacetect trecaactgg geaaaceceg ettecageag acgreetret arggeogetr caggeactre tregatarea regacecteg cacactetr greactgaga gacgreeteag agaggergre cagergergg aggacraraa gearggace ergegeeegg gggreaceaa rgaacagere rggagreac agaaaareaa geaggerarr eracareegg acaceaarga gaagaretre arg eea trr aga arg tea ggr tar	60 120 180 240 294
Met Pro Phe Arg Met Ser Gly Tyr  1 5 att cct ttt ggg acg cca att gta agt gtt acc ttc aaa gga ttt cct	342
Ile Pro Phe Gly Thr Pro Ile Val Ser Val Thr Phe Lys Gly Phe Pro 10 15 20 ttt cta aaa aat tat ttt aaa tgt cta act tta tgt tat tgc tca cgg	390
Phe Leu Lys Asn Tyr Phe Lys Cys Leu Thr Leu Cys Tyr Cys Ser Arg  35 40  qta ttt gac tgaattgttg att	412
Val Phe Asp	
<210> 53 <211> 597 <212> DNA <213> Homo sapiens	
<220> <221> CDS	
<221> sig_peptide <222> 103213 <223> Von Heijne matrix score 3.9 seq PGPSLRLFSGSQA/SV	
<221> polyA_site <222> 588597	
<400> 53 gaaaggtcag aggaaggagc tgtgggaagc tcgcagcagg tatcggagct taagccagtg gatttggggg ccctgggctc cctagccggc tgcggtgtga ga atg gag tgg gca Met Glu Trp Ala	60 114

WO 99/31236 -32 - PCT/IB98/02122

													_ :	3 5		
gga Gly	aag Lys	cag Gln	cgg ( Arg /	gac Asp	ttt d Phe d	ag g Sln V	/al /	agg g Arg <i>l</i>	gca g Ala <i>F</i>	gct c	ro C	Sly C	gg 9	gat o	at iis	162
ttg Leu	gcc Ala	tcc Ser -15	ttt	ect (	ggc ( Gly I	Pro 9	ct (	ctc	egg o	tg t Leu F	he S	ct ( Ser (	999 Gly	agt o	ag 31n	210
gcg Ala	agt Ser 1	gtc	tgt Cys	Ser	ctc ( Leu ( 5	cgc t	er (	ggg t	he C	999 9 31y <i>#</i>	gct o	cag q	gaa Glu			252
tctt ctct gaat aggg	gact aaaa cttt aaac	tt g ag c ta t tc c	caaa atca atgg agtg	acag tcta tttt aaaa cctt	t tgg g ctg a cti a tci	gato: tta: tgag! agcc	cac tta ttaa gctt	gcad cate gtte	eaaag cacto cgtco	gaa t ggc a ccc g cta g	ctga acagg gtggt gtgaa	aggte gata ggtt acac	gt t tt t tg t	tagad ttaca agtto	aattt ettca aggaa ettac ettgt	312 372 432 492 552 597
<211 <212	> 54 > 74 > DN > Ho	8 'A	apie	ns												,
	> .> CD :> 2.															
	> po			al											-	
<221 <222	.> pc		site	:												
	.> /3	57	48													
c ac	)> 54	i t co	t ct	u Le	c ct	a ga u Gl	g cc u Pr	t go	a As	p Hi	t gc s Al	c cg a Ar	jc gg rg Gl	ly Ar	nt gcc g Ala	49
c ac Th 1	)> 54 ca gt ir Va	t co il Pr cac	ct ct co Le cta Leu	u Le 5 CCT	c ct u Le gaa Glu	u Gl aat	u Pr gtt	cgc Arg	a As 10 agc	p Hi cag	s Al	a Ar	ggc Gly	ly Ar 15 cat	g Ala ; gtg	<b>49</b> 97
c ac Th 1 cat His	0> 54 ca gt or Va gtc Val	cac His	ct ct cta Leu 20	cct Pro	eu Le gaa	aat Asn qca	gtt Val cag Gln	cgc Arg 25 gta	a As 10 agc Ser cta	p Hi cag Gln ccg	s Al tct Ser	a Ar cct Pro gga Gly	ggc Gly 30 cct	ly Ar 15 cat His gat	g Ala gtg Val gag	
c ac Th 1 cat His cgc Arg	0> 54 ca gt r Va gtc Val agg Arg cag Gln	cac His ggc Gly 35	cta cta Leu 20 aga Arg	cct Pro agt Ser	gaa Glu	aat Asn gca Ala gaa Glu	gtt Val cag Gln 40 gtt	cgc Arg 25 gta Val	a As 10 agc Ser cta Leu ttc	p Hi cag Gln ccg Pro	s Al tct Ser acc Thr	a Ar cct Pro gga Gly 45 tca	ggc Gly 30 cct Pro	ty Ar 15 cat His gat Asp	g Ala gtg Val gag Glu	97
c ac Th 1 cat His cgc Arg aaa Lys	0> 54 ca gtc yal agg Arg cag Gln 50	cac His ggc Gly 35 gtt Val	ct ct cta Leu 20 aga Arg gag Glu	eu Le 5 cct Pro agt Ser aag Lys	gaa Glu ggt Gly agt Ser gat Asp	aat Asn gca Ala gaa Glu 55	gtt Val cag Gln 40 gtt Val	cgc Arg 25 gta Val gat Asp	a As 10 agc Ser cta Leu ttc Phe aag	p Hi cag Gln ccg Pro tca ser	s Al tct Ser acc Thr aag Lys 60 tct	a Ar cct Pro gga Gly 45 tca Ser	ggc Gly 30 cct Pro cat His	ly Ar 15 cat His gat Asp agc Ser	g Ala gtg Val gag Glu tta Leu	97 145 193 241
c ac Th 1 Cat His cgc Arg aaa Lys gtg Val 65	0> 54 ca gtc val agg Arg cag Gln so aga Arg	cac His GGly 35 Gtt Val cga Arg	ct ct cta Leu 20 aga Arg gag Glu ttt Phe	cct Pro agt Ser aag Lys gag Glu ttt	gaa Glu ggt Gly agt Ser	aat Asn gca Ala gaa Glu 55 ctg Leu	gtt Val cag Gln 40 gtt Val aag Lys	cgc Arg 25 gta Val gat Asp ccc Pro aac	a As 10 agc Ser cta Leu ttc Phe aag	p Hi cag Gln ccg Pro tca Ser ctt Leu 75 aag	tct Ser acc Thr aag Lys 60 tct Ser	a Ar cct Pro gga Gly 45 tca Ser gtt Val	ggc Gly 30 cct Pro cat His tgc Cys	cat His gat Asp agc Ser aaa Lys	g Ala gtg Val gag Glu tta Leu act Thr 80 tcg	97 145 193
c ac Th 1 cat His cgc Arg aaa Lys gtg Val 65 gga Gly agc Ser	o> 54 ca gtc val gtc val agg Arg cag Gln 50 aga Arg tca Ser aga	cac His ggc Gly 35 gtt Val cga Arg caa Gln	ct ct cta Leu 20 aga Arg Glu ttt Phe gtc Val gac Asp	eu Le 5 CCC Pro agt Ser aag Lys gag Glu ttt Phe 85 cat His	gaa Glu ggt Gly agt Ser gat Asp 70 cgg Arg	aat Asn gca Ala gaa Glu 55 ctg Leu tcg Ser gac Asp	u Pr gtt Val cag Gln 40 gtt Val aag Lys gag Glu tgc	cgc Arg 25 gta Val gat Asp ccc Pro aac Asn cta Leu 105	a As 10 agc Ser cta Leu ttc Phe aag Lys tgg Trp 90 gac Asp	p Hi cag Gln ccg Pro tca Ser ctt Leu 75 aag Lys ttg Leu	s All tet Ser acc Thr aag Lys 60 tet Ser gtc Val tgc Cys	a Ar cct Pro gga Gly 45 tca Ser gtt Val tgg Trp tca Ser	ggc Gly 30 cct Pro cat His gca Ala gtg Val	cat His gat Asp agc Ser aaa Lys Glu 95 ctg	gtg Val gag Glu tta Leu act Thr 80 tcg Ser	97 145 193 241 289
c ac Th 1 cat His cgc Arg aaa Lys gtg Val 65 gga Gly agc Ser	0> 54 ca gtc val agg Arg cag Gln so aga Arg tca Ser aga	cac His ggc Gly 35 gtt Val cga Arg Gln gga Gly	ct ct cta Leu 20 aga Arg Glu ttt Phe gtc Val gac Asp	eu Le 5 CCCT Pro agt Ser aag Lys gag Glu ttt Phe 85 cat His	gaa Glu ggt Gly agt Ser gat Asp 70 cgg Arg	aat Asn gca Ala gaa Glu 55 ctg Leu tcg Ser gac Asp	u Pr gtt Val cag Gln 40 gtt Val aag Lys gag Glu tgc Cys	cgc Al cgc Arg 25 gta Val gat Asp ccc Pro aac Leu 105 cct Pro	a As 10 agc Ser cta Leu ttc Phe aag Lys tgg Trp 90 gac Asp gaa	p Hi cag Gln ccg Pro tca Ser ctt Leu 75 aag Lys ttg Leu att	s All tet Ser acc Thr aag Lys 60 tet Ser gtc Val tgc Cys	a Ar cct Pro gga Gly 45 tca Ser gtt Val tgg Trp tca Ser cca	ggc Gly 30 cct Pro cat His tgc Cys gca Ala gtg Val	cat His gat Asp agc Ser aaa Lys Glu 95 ctg Leu cgt	g Ala gtg Val gag Glu tta Leu act Thr 80 tcg Ser	97 145 193 241 289

caa gtt tot caa cag gag gaa ott aaa taactatgoo aagaattotg Gln Val Ser Gln Gln Glu Glu Leu Lys	480
tgaataatat aagtottaaa tatgtattoo ttaatttatt goatcaaact acttgtoott aagcacttag totaatgota actgcaagag gaggtgotca gtggatgttt agcogatacg ttgaaattta attacggttt gattgatatt tottgaaaac ogcoaaagca catatoatca aaccatttoa tgaatatggt ttggaagatg tttagtottg aatataatgo gaaatagaat atttgtaagt otaccaaaaa aaaaaaaa	540 600 660 720 748
<210> 55 <211> 703 <212> DNA <213> Homo sapiens	
<220> <221> CDS	
<221> CDS <222> 31231	
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 769774</pre>	
<221> polyA_site <222> 690703	
<400> 55 ctctggtggc tctgctacgg cggcgcagaa atg agg cag aag cgg aaa gga gat Met Arg Gln Lys Arg Lys Gly Asp 1 5	54
ctc agc cct gct aag ctg atg atg ctg act ata gga gat gtt att aaa Leu Ser Pro Ala Lys Leu Met Met Leu Thr Ile Gly Asp Val Ile Lys 10 15 20	102
caa ctg att gaa gcc cac gag cag ggg aaa gac atc gat cta aat aag Gln Leu Ile Glu Ala His Glu Gln Gly Lys Asp Ile Asp Leu Asn Lys 25 30 35	150
qtq aga acc aag aca gct gcc aaa tat ggc ctt tct gcc cag ccc cgc	198
Val Arg Thr Lys Thr Ala Ala Lys Tyr Gly Leu Ser Ala Gln Pro Arg 50 55	
ctg gtg gat atc att gct gcc gtc cct cct gag tagctgggat tacaggcacc Leu Val Asp Ile Ile Ala Ala Val Pro Pro Glu  60 65	251
cgccqctqcc aatttttgta tttttagtag ggatgggggt ttcaccatat tggtcaggct	311
ggtctcgaac tcctgacctc aggtgatcaa cccaccttgg cctccctaaa tgccgggatt	371
acaggcatga gccaccgete egggcetttg attttttaag gtggattttg gttgttataa	431
atggagaaag gtaagagtte aagtteaace egtgtgtgaa ageaaaacaa tggaaaacag gattggette tteaaagget eetettgtag aactgeetet ttgaaattte gaggtaatet	551
actitiggaga ctctgcctgg agagggtcag ttcctaagtt aaaagcatcg cttaaccttg	611
geteetgtgg cattttacaa aggtttaaag gaattgatte etetgaaagg geetgaaaat	671
aaaaagtctt taacatacaa aaaaaaaaaaa aa	703
<210> 56	
<211> 725 <212> DNA	

<212> DNA <213> Homo sapiens

<220>

<221> CDS

<222> 305..565

<221> polyA_signal	
<221> polyA_site   <222> 713725	
<400> 56 ctcacggtgg tgaaggtcac agggttgcag cactcccagt agaccaggag ctccgggagg cagggccggc cccacgtcct ctgcgcacca ccctgagttg gatcctctgt gcgccacccc tgagttggat ccagggctag ctgctgttga cctcccact cccacgctgc cctcctgcct gcagccatga cgccctgct caccctgatc ctggtggtc tcatgggct acctctggcc caggccttgg actgccacgt gtgaggacta caaatccctc caggatatca ttgccatcct gggt atg gat gaa ctt tct gag gaa gac aag ttg acc gtg tcc cgt gca  Met Asp Glu Leu Ser Glu Glu Asp Lys Leu Thr Val Ser Arg Ala  1 5 10	60 120 180 240 300 349
cgg aaa ata cag cgt ttc ttg tct cag cca ttc cag gtt gct gag gtc Arg Lys Ile Gln Arg Phe Leu Ser Gln Pro Phe Gln Val Ala Glu Val 20 25 30	397
ttc aca ggt cat atg ggg aag ctg gta ccc ctg aag gag acc atc aaa Phe Thr Gly His Met Gly Lys Leu Val Pro Leu Lys Glu Thr Ile Lys 35 40 45	445
gga ttc cag cag att ttg gca ggt gaa tat gac cat ctc cca gaa cag Gly Phe Gln Gln Ile Leu Ala Gly Glu Tyr Asp His Leu Pro Glu Gln 50 55 60	493
gcc ttc tat atg gtg gga ccc att gaa gaa gct gtg gca aaa gct gat Ala Phe Tyr Met Val Gly Pro Ile Glu Glu Ala Val Ala Lys Ala Asp 65 70 75	541
aag ctg gct gaa gag cat tca tcg tgaggggtct ttgtcctctg tactgtctct Lys Leu Ala Glu Glu His Ser Ser 80 85	595
ctccttgccc ctaacccaaa aagcttcatt tttctgtgta ggctgcacaa gagccttgat tgaagatata ttctttctga acagtattta aggtttccaa taaagtgtac acccctcaaa aaaaaaaaaa	655 715 725
<210> 57 <211> 1705 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 124873	
<221> sig_peptide <222> 124378 <223> Von Heijne matrix score 3.6 seq HLSVVTLAAKVKC/IP	
<221> polyA_signal	
<221> polyA_site <222> 16941705	
<400> 57 cggaggtgag gagcggcggc cccgcccggt gcgctggagg tcgaagcttc caggtagcgg cccgcagagc ctgacccagg ctctggacat cctgagccca agtccccac actcagtgca gtg atg agt gcg gaa gtg aag gtg aca ggg cag aac cag gag caa ttt Met Ser Ala Glu Val Lys Val Thr Gly Gln Asn Gln Glu Gln Phe	6 12 16

	- 85					-80					- 75					
cta		cta	acc	aaq	tċa		aaq	qqq	qca	qcq		qcc	aca	ctc	atc	216
Leu	Leu	Leu	Ala	Lys	Ser	Ala	Lys	Gly	Ala	Ala	Leu	Ala	Thr	Leu	Ile	
-70				•	-65		•			-60					-55	
cat	cag	gtg	ctg	gag	gcc	cct	ggt	gtc	tac	gtg	ttt	gga	gaa	ctg	ctg	264
His	Gln	Val	Leu	Glu	Ala	Pro	Gly	Val	Tyr	Val	Phe	Gly	Glu	Leu	Leu	
				-50					-45					-40		
gac	atg	ccc	aat	gtt	aga	gag	ctg	naa	gcc	cgg	aat	ctt	cct	cca	cta	312
Asp	Met	Pro	Asn	Val	Arg	Glu	Leu	Xaa	Ala	Arg	Asn	Leu		Pro	Leu	
			-35					-30					-25			
aca	gag	gct	cag	aag	aat	aag	ctt	cga	cac	ctc	tca	gtt	gtc	acc	ctg	360
Thr	Glu		Gln	Lys	Asn	Lys		Arg	His	Leu	Ser		Val	Thr	Leu	
		-20					-15					-10				400
gct	gct	aaa	gta	aag	tgt	atc	cca	tat	gca	gtg	ttg	ctg	gag	gct	CCC	408
Ala		rys	Val	Lys	Cys		Pro	TYT	Ala	vai	Leu	Leu	GIU	Ala	10	
	-5					1		~~~	~~~	3 2++	a= a		<b>~</b> 3~	act		456
gcc	ctg	cgt	aat	gtg	cgg	cag	tou	Clu	yac	Len	Val	Tla	Glu	gct Ala	Val	430
Ald	neu	Arg	ASII	15	Arg	GIII	Deu	GIU	20	пси	141	110	014	25	• • • • • • • • • • • • • • • • • • • •	
+=+	act	<b>G</b> = <b>C</b>	ata		cat	aac	tcc	cta		cag	cac	aac	cag	cgg	ctc	504
Tur	Mla	yac Aen	yey val	T.AII	Ara	Glv	Ser	Leu	Asp	Gln	Ara	Asn	Gln	Arg	Leu	•
ı y ı	A14	vob	30	Deu	7.9	O.J	001	35					40	5		
gag	att	gac		agc	atc	aaa	caa		atc	caq	cqc	caq	gac	ctc	agt	552
Glu	Val	Asp	Tvr	Ser	Ile	Glv	Arg	Asp	Ile	Gln	Arg	Gln	Asp	Leu	Ser	
		45	-1-			2	50	•			•	55	-			
acc	att	acc	cqa	acc	ctq	cag	gaa	tgg	tgt	gtg	ggc	tgt	gag	gtc	gtg	600
Ala	Ile	Ala	Arq	Thr	Leu	Gln	Glu	Trp	Cys	Val	Gly	Cys	Glu	Val	Val	
	60		•			65		_	•		70					
ctg	tca	ggc	att	gag	gag	cag	gtg	agc	cgt	gcc	aac	caa	cac	aag	gag	648
Leu	Ser	Gly	Ile	Glu	Glu	Gln	Val	Ser	Arg	Ala	Asn	Gln	His	Lys	Glu	
75					80					85					90	
cag	cag	ctg	ggc	ctg	aag	cag	cag	att	gag	agt	gag	gtt	gcc	aac	ctt	696
Gln	Gln	Leu	Gly	Leu	Lys	Gln	Gln	Ile			Glu	Val	Ala	Asn	Leu	,
				95					100					105		744
aaa	aaa	acc	att	aaa	gtt	acg	acg	gca	gca	gca	gcc	gca	gcc	aca	Com	744
Lys	Lys	Thr		Lys	Val	Thr	Thr			Ala	Ата	Ата		Thr	Ser	
			110					115					120		666	792
cag	gac	CCE	gag	caa	cac	ctg	act	gag	tou	agg	yaa Glu	Dro	, gcc	Dro	ggc	
GIn	Авр		GIU	GIn	HIS	Leu	130		пел	Arg	GIU	135		PIO	Gly	
	224	125		~~~		200			acc	tca	220				ctc	840
The	Agn	Gla	Ara	Gln	Pro	Ser	Lvs	Lvs	Ala	Ser	Lve	Glv	Lvs	Glv	Leu	
1111	140	GIII	nr 9	GIII		145		-,-			150		-,-			
cga		age	acc	аад	att			aaq	tco	aat	tqa	aaqa	act	gtcg	stttcct	893
Ara	Glv	Ser	Ala	Lys	Ile	Trp	Ser	Lys	Ser	Asn	1	-				
155				-, -	160			•		165	<b>i</b>					
		qat	ataa	aatc	cc a	gctg	cctg	c ct	gcct	ctta	gga	gtc	ctca	gaga	agcette	953
tat	accc	ctq	qcca	gctg	at a	atco	tagg	t to	atga	accet	tca	acct	ccc	taac	cccaaa	1013
cat	agat	cac	acct	tctc	ta q	ggag	gagt	c aa	atgt	aggt	: cat	tgtti	tttg	ttgg	gtacttt	1073
ctq	tttt	ttg	tgac	ttca	tg t	gtto	catt	g ct	CCC	gctg	g cca	atgc	tctc	tcc	cttgttt	1133
cct	taag	agc	tcag	cato	tg t	ccct	gttc	a tt	aca	tgtca	a tt	gagt	aggt	9991	tagccct	1193
gat	9999	gtc	gcto	tgto	tg g	agca	taac	c ca	acag	gcgtt	t tt	ttct	gcca	CCC	catccct	1253
gca	tgcc	tga	tccc	cagt	tc c	tata	accet	a co	cct	gacct	t at	tgag	cagc	ctc	tgaagag	1313
cca	tagg	qcc	ccca	cctt	tac	tcac	cacco	et ga	agaa	ttct	3 33	agcc	agtc	tgc	catgcca	1373
qqa	qtca	ctg	gaca	tgtt	ca t	ccta	igaat	C -C1	tgtc	acact	t ac	agtc	attt	ctt	ttcctct	1433
CtC	taac	cct	taga	tcct	gg c	jaato	gctgo	et go	cttc	aacc	c ca	gagc	ctaa	gaa	tggcagc	1493
cgt	ttct	taa	cato	gttga	aga g	gatga	attct	t to	cttg	gccc	t gg	ccat	ctcg	gga	agcttga	1553
tgg	caat	cct	ggaa	gggt	tt a	atct	tectt	tt to	gtga	gttt	g gt	<b>3</b> 333	aagg	gaa	gggtata	1613
tag	atta	tat	taaa	aaaa	aaa a	aggı	tatat	ta t	gcat	atat	c ta	tata	taat	atg	acgcaga	1673 1705
aat	aaat	cta	tgag	gaaat	cc a	aaaa	aaaa	aa a	a							1/05

```
<210> 58
<211> 1069
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 135..206
<221> polyA signal
<222> 850..855
<221> polyA_site
<222> 1056..1069
<400> 58
cocactoogo totoacgact aagototoac gattaaggoa egeotgooto gattgiocag
                                                                      60
cetetgecag aagaaagett ageagecage geeteagtag agacetaagg gegetgaatg
                                                                     120
agtgggaaag ggaa atg ccg acc aat tgc gct gcg gcg ggc tgt gcc act
                                                                     170
                Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr
                                                                     216
acc tac aac aag cac att aac atc agc ttc cac agg taacctgggc
Thr Tyr Asn Lys His Ile Asn Ile Ser Phe His Arg
                            20
agggagtggg ggtgacggaa actggagttc ctattgtggc tatcgcttgt gtggaaggaa
                                                                     276
caggaggatt ctgctaattc taataacttt cccagctggt agcagggaag catcgtatgt
                                                                     336
                                                                     396
cotttgtgtt totcaaatot goccaattgt tototgettt cggggaaget ttactcattt
                                                                     456
tctaaaagaa atccaagtac tgtttggtca ttacccctta gtaaaaaaa gtaacaggag
gatatogtaa ttttotactg ttttattoot otgttagaco gggoottgac atgaatgacg
                                                                     516
                                                                     576
ccgtaaggga gaaagagatc ttcccaatca gcaatcaccg taaaagcctg ctgtgttccc
gttaaaatta ggaaattoto actagatgaa ttgacatggg aggcatttag atttotaata
                                                                      636
gtcacatagt aattetgegg aggaattgag teatetttga tageeatgga attaagegat
                                                                      696
gttaattaaa gtgcaaacga taacctttct gttcttacta gaatagagta ataaaaagaa
                                                                      756
cctaggtttt cttttgtttg ctggaagaaa aatcaaaatt ctttagttct gtcaaaccag
                                                                      816
                                                                      876
aactettgaa ageaetttga acaatgeetg gaaaataaca ggtaetetgt aaatgtttae
cttctctgca agtgcctgcc acgtgcccga agaaaagaca cattaaaaag ttaagtgaca
                                                                      936
ccagtcctga ttttatatat tttatatacc taacaacgta tatgttagta tgtagaaatt
                                                                      996
                                                                     1056
atateettga cetttttece tacetattae gaactgtaet tetattaaaa getgeeacta
                                                                     1069
aaaaaaaaa aaa
<210> 59
<211> 1084
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 135..818
<221> polyA_signal
<222> 909..914
<221> polyA_site
<222> 1071..1084
 <400> 59
                                                                       60
occactoogo totoacgact aagototoac gattaaggoa ogcotgooto gattgtocag
cetetgecag aagaaagett ageagecage geeteagtag aggeetaagg gegetgaatg
                                                                       120
agtgggaaag ggaa atg ccg acc aat tgc gct gcg ggc tgt gcc act
                                                                       170
```

				Met	Pro	Thr	Asn	Cys	Ala	Ala	Ala	Gly	Cys	Ala	Thr	
				1				5					10	<b></b> -		210
		aac												_	-	218
Thr	Tyr	Asn	Lys	His	Ile	Asn		ser	Phe	His	Arg		Pro	Leu	Asp	
		15					20					25				
cct	aaa	aga	ag <b>a</b>	aaa	gaa	tgg	gtt	cgc	ctg	gtt	agg	cgc	aaa	aat	ttt	266
Pro	Lys	Arg	Arg	Lys	Glu	Trp	Val	Arg	Leu	Val	Arg	Arg	Lys	Asn	Phe	
	30					35					40					
gtg	cca	gga	aaa	cac	act	ttt	ctt	tgt	tca	aag	cac	ttt	gaa	gcc	tcc	314
Val	Pro	Gly	Lvs	His	Thr	Phe	Leu	Cvs	Ser	Lvs	His	Phe	Glu	Āla	Ser	
45		•	•		50			•		55					60	
	+++	gac	cta	aca		caa	act	cga	спа		222	ato	gat	act		362
_		Asp						_	-			-		_	-	300
Cys	FIIC	Asp	neu		GIY	GIII	1111	ALG	_	Ded	nya	Mec	АБЪ		441	
				65					70					75		430
		att		-		_				_		_			-	410
Pro	Thr	Ile	Phe	Asp	Phe	Cys	Thr	His	Ile	Lys	Ser	Met	Lys	Leu	Lys	
			80					85					90			
tca	agg	aat	ctt	ttg	aag	aaa	aac	aac	agt	tgt	tct	cca	gct	gga	cca	458
Ser	Arg	Asn	Leu	Leu	Lys	Lys	Asn	Asn	Ser	Cys	Ser	Pro	Ala	Gly	Pro	
	_	95			•	•	100			•		105		_		
tet	agt	tta	aaa	tca	aac	att		agt	cag	caa	αta	cta	ctt	gaa	cac	506
Ser	Ser	Leu	Lve	Ser	Aen	Tle	Ser	Ser	Gln	Gln	Val	Leu	Len	Glu	Hig	-
Jer	110	пси	цуз	Jer	7311	115	561	JCI	0111	0111	120	200		014		
																554
		gcc														224
	Tyr	Ala	Phe	Arg		Pro	Met	GIU	АТА	-	ràs	Arg	TIE	iie	-	
125					130					135					140	
		aaa														602
Leu	Glu	Lys	Glu	Ile	Ala	Ser	Leu	Arg	Arg	Lys	Met	Lys	Thr	Cys	Leu	
				145			,		150					155		
caa	aaq	gaa	cqc	aga	qca	act	cga	aga	tgg	atc	aaa	gcc	atg	tgt	ttg	650
Gln	Lvs	Glu	Arg	Ara	Ala	Thr	Arq	Arq	Trp	Ile	Lys	Ala	Met	Cys	Leu	
	-7 -		160	5			3	165					170	•		
at a	220	aat		~~~	~~~	22F	agt		tta	cct	222	aat		tca	gaa	698
		Asn														
val	.Lys		reu	Giu	MIG	WPII		V 4.1	neu	PLO	Ly S	185	1111	561	014	
		175					180									716
		tta														746
His	Met	Leu	Pro	Thr	Ala	Leu	Ser	Ser	Leu	Pro	Leu	Glu	Asp	Phe	Lys	
	190					195					200					
atc	ctt	gaa	caa	gat	caa	caa	gat	aaa	aca	ctg	cta	agt	cta	aat	cta	794
Ile	Leu	Glu	Gln	Asp	Gln	Gln	Asp	Lys	Thr	Leu	Leu	Ser	Leu	Asn	Leu	
205				•	210		•	•		215					220	
	cag	acc	аад	agt		ttc	att	taa	attt	age	ttac	acag	ag c	ttga	tgcct	848
			_	_			_			-90		5	-5 -		-3	
пåя	GIII	Thr	nys		1111	FILE	TIE						•		,	
				225										<b></b>		908
atc	CTTC	att o	ctt	ccag	aa g	caaa	gata	a tt	atgg	cact	tat	gcca	aaa	ctca	ttattt	
aat	aaag	ttt 1	tact	tgaa	gt a	acat	tact	g aa	tttg	tgaa	gac	ttga	tta	caaa	agaata	968
aaa	aact	tca 1	tatg	gaaa	tt t	tatt	tgaa	a at	gagt	ggaa	gcg	cctt	aca	ttag	aattac	1028
gga	ctta	aaa a	attt	tgct	aa t	aaat	tgtg	t gt	ttga	aagg	tga	aaaa	aaa	aaaa	aa	1084
				_												

<211> 419

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 33..290

<221> sig_peptide ·

<222> 33..92

<223> Von Heijne matrix score 5.4 seq WFVHSSALGLVLA/PP <400> 60 aatggtagge etteatgtga geeagttaet ac atg aat ett eat tte eea eag Met Asn Leu His Phe Pro Gln -20 tgg ttt gtt cat tca tca gcg tta ggc ttg gtc ctg gct cca cct ttc 101 Trp Phe Val His Ser Ser Ala Leu Gly Leu Val Leu Ala Pro Pro Phe -5 tcc tct ccg ggc act gac ccc acc ttt ccg tgt att tac tgt agg cta 149 Ser Ser Pro Gly Thr Asp Pro Thr Phe Pro Cys Ile Tyr Cys Arg Leu 10 tta aat atg atc atg acc cgc ctt gca ttt tca ttc atc acc tgt tta 197 Leu Asn Met Ile Met Thr Arg Leu Ala Phe Ser Phe Ile Thr Cys Leu 30 245 tgc cca aat tta aag gaa gtt tgt ctc att ttg cca gaa aaa aat tgt Cys Pro Asn Leu Lys Glu Val Cys Leu Ile Leu Pro Glu Lys Asn Cys 45 40 aat agt cgg cac gct gga ttt gta ggg cca gca aaa ttg cgg cag 290 Asn Ser Arg His Ala Gly Phe Val Gly Pro Ala Lys Leu Arg Gln 60 350 tgaaactagt ttcacttcta aagcccttca tttcccacaa ggttaagctc tcgaaacccc atttgatect tggttectat ttegatecte etttggaate tgaaaategg tetecatgtt 410 419 gtatgcaaa <210> 61 <211> 682 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 485..616 <221> polyA_site <222> 669..682 <400> 61 ctcctttctc attccttatc ttgcgtgttt ttaccttttt ttcataacta agtttttgag 60 gaagttagtg ttcttttcaa agaaccggtt cgaaatgtac ttttctttgc tactttttgt 120 180 tattttattg atcacatctt taatcttttg ttctctatac gtggcctgtt ttgatttatt 240 ttactattct tgctttctaa ggtaagtatt ttgttgtgta gtgctttatt tttttcatct ttottottga ataataatga catttttagg ttataaattt toototggta ctcagtttgc 300 360 ctcattaatt ttggcagtaa gcattctcct tttattgctt tctatgtagt ctttaatttt gettttaact tettetttga tetaaggatt acctaettgt taattteeaa atattatett 420 480 gget atg teg eeg agg etg gag tge agt ggt gea ate ttg get eac tge 529 Met Ser Pro Arg Leu Glu Cys Ser Gly Ala Ile Leu Ala His Cys 10 aac cee ege etc cea ggt tea agt tat tet eet gee tea get aet tgg 577 Asn Pro Arg Leu Pro Gly Ser Ser Tyr Ser Pro Ala Ser Ala Thr Trp 25 20 gtg aga gga tcc ctt gag ccg ggg agg ttg agg ctg cag tgagccataa 626 Val Arg Gly Ser Leu Glu Pro Gly Arg Leu Arg Leu Gln 40 682 ccactactct ccagcctgga taacaaaagt gagactctga ccaaaaaaaa aaaaaa

```
<210> 62
<211> 1191
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 54..995
<221> sig_peptide
<222> 54..227
<223> Von Heijne matrix
     score 4.1
     seq LVHHCPTWQWATG/EE
<221> polyA_signal
<222> 1130..1135
<221> polyA_site
<222> 1181..1191
<400> 62
cacggctgca ctttccatcc cgtcgcgggg ccggccgcta ctccggcccc agg atg
                                                                      56
                                                                     104
cag aat gtg att aat act gtg aag gga aag gca ctg gaa gtg gct gag
Gln Asn Val Ile Asn Thr Val Lys Gly Lys Ala Leu Glu Val Ala Glu
                            -50
                                                                     152
tac ctg acc ccg gtc ctc aag gaa tca aag ttt agg gaa aca ggt gta
Tyr Leu Thr Pro Val Leu Lys Glu Ser Lys Phe Arg Glu Thr Gly Val
                                            - 30
                        -35
att acc cca gaa gag ttt gtg gca gct gga gat cac cta gtc cac cac
                                                                     200
Ile Thr Pro Glu Glu Phe Val Ala Ala Gly Asp His Leu Val His His
                    -20
                                        -15
                                                                     248
tgt cca aca tgg caa tgg gct aca ggg gaa gaa ttg aaa gtg aag gca
Cys Pro Thr Trp Gln Trp Ala Thr Gly Glu Glu Leu Lys Val Lys Ala
                - 5
tac cta cca aca ggc aaa caa ttt ttg gta acc aaa aat gtg ccg tgc
                                                                      296
Tyr Leu Pro Thr Gly Lys Gln Phe Leu Val Thr Lys Asn Val Pro Cys
                            15
                                                                      344
tat aag egg tge aaa cag atg gaa tat tea gat gaa ttg gaa get ate
Tyr Lys Arg Cys Lys Gln Met Glu Tyr Ser Asp Glu Leu Glu Ala Ile
                        30
att gaa gaa gat gat ggt gat ggc gga tgg gta gat aca tat cac aac
                                                                      392
Ile Glu Glu Asp Asp Gly Asp Gly Trp Val Asp Thr Tyr His Asn
                                         50
                     45
                                                                      440
aca ggt att aca gga ata acg gaa gcc gtt aaa gag atc aca ctg gaa
Thr Gly Ile Thr Gly Ile Thr Glu Ala Val Lys Glu Ile Thr Leu Glu
                                     65
                 60
aat aag gac aat ata agg ctt caa gat tgc tca gca cta tgt gaa gag
                                                                      488
Asn Lys Asp Asn Ile Arg Leu Gln Asp Cys Ser Ala Leu Cys Glu Glu
                                                    85
                                 80
gaa gaa gat gaa gaa gga gaa gct gca gat atg gaa gaa tat gaa
                                                                       536
Glu Glu Asp Glu Asp Glu Gly Glu Ala Ala Asp Met Glu Glu Tyr Glu
                                                 100
         90
                             95
                                                                       584
gag agt gga ttg ttg gaa aca gat gag gct acc cta gat aca agg aaa
Glu Ser Gly Leu Leu Glu Thr Asp Glu Ala Thr Leu Asp Thr Arg Lys
                                             115
                         110
                                                                       632
 ata gta gaa gct tgt aaa gcc aaa act gat gct ggc ggt gaa gat gct
Ile Val Glu Ala Cys Lys Ala Lys Thr Asp Ala Gly Gly Glu Asp Ala
                     125
                                         130
 att ttg caa acc aga act tat gac ctt tac atc act tat gat aaa tat
                                                                       680
```

Ile Leu Gln Thr Arg Thr Tyr Asp Leu Tyr Ile Thr Tyr Asp Lys Tyr 140 145 150	
tac cag act cca cga tta tgg ttg ttt ggc tat gat gag caa cgg cag	728
Tyr Gln Thr Pro Arg Leu Trp Leu Phe Gly Tyr Asp Glu Gln Arg Gln	
155 160 165	
cot tha aca git gag cac ang tat gaa gac and agt cag gat cat gig	776
Pro Leu Thr Val Glu His Met Tyr Glu Asp Ile Ser Gln Asp His Val	
170 175 180	
aag aaa aca gtg acc att gaa aat cat cct cat ctg cca cca cct ccc	824
Lys Lys Thr Val Thr Ile Glu Asn His Pro His Leu Pro Pro Pro	
185 190 195	
atg tgt tca gtt cac cca tgc agg cat gct gag gtg atg aag aaa atc	872
Met Cys Ser Val His Pro Cys Arg His Ala Glu Val Met Lys Lys Ile	
200 205 210 215	
att gag act gtt gca gaa gga ggg gga gaa ctt gga gtt cat atg tat	920
Ile Glu Thr Val Ala Glu Gly Gly Glu Leu Gly Val His Met Tyr	
220 225 230	
220	968
ctt ctt att ttc ttg aaa ttt gta caa gct gtc att cca aca ata gaa	200
Leu Leu Ile Phe Leu Lys Phe Val Gln Ala Val Ile Pro Thr Ile Glu	
235 240 245	1015
tat gac tac aca aga cac ttc aca atg taatgaagag agcataaaat	1015
Tyr Asp Tyr Thr Arg His Phe Thr Met	
250 255	
ctatcctaat tattggttct gatttttaaa gaattaaccc atagatgtga ccattgacca	1075
tattcatcaa tatatacagt ttctctaata agggacttat atgtttatgc attaaataaa	1135
aatatgttcc actaccagcc ttacttgttt aataaaaatc agtgcaaaaa aaaaaa	1191

<211> 1008

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 657..923

<221> sig_peptide

<222> 657..896

<223> Von Heijne matrix score 3.5 seq RGLLSACAPWGDG/ST

<221> polyA_signal

<222> 957..962

<221> polyA_site

<222> 974..1008

<400> 63 ntcgnatgtg gcacaaaacc cctctgctgg ctcatgtgtg caactgagac tgtcagagca 120 tggctagctc tggggtccag ctctgctggg tggggggctag agaggaagca gggagtatct 180 geacacagga tgeetgeget caggtggttg cagaagteag tgeecaggee eccecacaca gtccccaaag gtccggcctc cccagcgcgg ggctcctcgt ttgaggggag gtgacttccc 240 teccageagg etettggaca cagtaagett ecceageeet geetgageag cettteetee ttgccctgtt ccccacctcc cggctccagt ccagggagct cccagggaag tggtcgaccc 360 420 ctccagtggc tgggccactc tgctagagtc catccgccaa gctgggggca tcggcaaggc caagetgege ageatgaagg agegaaaget ggagaagaag aageagaagg ageaggagea 480 540 agtgagagcc acgagccaag gtgggcactt gatgtcggat ctcttcaaca agctggtcat 600 gaggcgcaag ggcatctctg ggaaagaacc tggggctggt gaggggcccg gaggagcctt 659 tgcccgcgtg tcagactcca tccctcctct gccgccaccg cagcagccac aggtag atg

Thr Ser Glu Pro Leu Thr Ala

	•
Met -80	
agg aca agg acg act ggg aat cct agg ggg ctc cat gac acc ttc ccc Arg Thr Arg Thr Thr Gly Asn Pro Arg Gly Leu His Asp Thr Phe Pro -75 -70 -65	707
cgc aga ccc aga ctt ggc cgt tgc tct gac atg gac aca gcc agg aca Arg Arg Pro Arg Leu Gly Arg Cys Ser Asp Met Asp Thr Ala Arg Thr -60 -55 -50	755
age tgc tca gac ctg ctt ccc tgg gag gtg acg gaa cca gca ctg Ser Cys Ser Asp Leu Leu Pro Trp Glu Gly Val Thr Glu Pro Ala Leu -45 -40 -35	803
tgt gga gac cag ctt caa gga acg gaa ggc tgg ctt gag gcc aca cag Cys Gly Asp Gln Leu Gln Gly Thr Glu Gly Trp Leu Glu Ala Thr Gln -30 -25 -20	851
ctg ggg cgg gga ctt ctg tct gcc tgt gct cca tgg ggg gac ggc tcc Leu Gly Arg Gly Leu Leu Ser Ala Cys Ala Pro Trp Gly Asp Gly Ser -15 -5 1	899
acc cag cct gtg cca ctg tgt tct taagaggett ccagagaaaa cggcacacca Thr Gln Pro Val Pro Leu Cys Ser	953
atcaataaag aactgagcag aaaaaaaaaa aaaaaaaaaa	1008
<210> 64 <211> 568	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS <222> 18311	
2007. Air mampida	
<221> sig_peptide <222> 1862	
<223> Von Heijne matrix	
score 8.4 seq AMWLLCVALAVLA/WG	
<400> 64	50
agtgctgctt acceate atg gaa gea atg tgg etc etg tgt gtg geg ttg  Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu  -15 -10 -5	50
gcg gtc ttg gca tgg ggc ttc ctc tgg gtt tgg gac tcc tca gaa cga Ala Val Leu Ala Trp Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg 1 5 10	98
atg aag agt cgg gag cag gga gga cgg ctg gga gcc gaa agc cgg acc	146
Met Lys Ser Arg Glu Gln Gly Gly Arg Leu Gly Ala Glu Ser Arg Thr 15 20 25	• • •
ctg ctg gtc ata gcg cac cct gac gat gaa gcc atg ttt ttt gct ccc Leu Leu Val Ile Ala His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro	194
30 35 40	
aca gtg cta ggc ttg gcc cgc cta agg cac tgg gtg tac ctg ctt tgc	242
Thr Val Leu Gly Leu Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys 45 50 60	
tto tot goa gtt tto ogt agg gag ota agt gaa tac acc gaa ggt ott	290
Phe Ser Ala Val Phe Arg Arg Glu Leu Ser Glu Tyr Thr Glu Gly Leu 65 70 75	
acc tot gaa coo oto aca goo tagggacagg agoggooggo ttacotggtg	341
The Car Clu Dro Lau The Ala	

ggttggggga cgtcggcagc tcgcgtacta cgccagcagg attgaggagc agagaaacag

-41-

461

ttgcagttgg ttgtattcag tacctgcatt tccgttggga actccacctg tacttgttat

									agaat						gcaca	521
cgaaa	acaa	tc t	atqc	tqta	t ca	tacc	tact	caa	tectt	aa	agtt	aac			_	568
- <b>944</b>		-	3	- 3	5	• 5 • •	- 3									
<210:	> 65															
<211:		8														
<212:																
<213:			apie	ns												,
<220:																
<221:	> CD	S														
<222:	> 15	14	26													
<221:	- si	a ne	ptid	e												
<222:			_	_												
<223:				mat	rix											
~223.		ore	-													
			ALAG	LLGF	GLG/	ΚV										
		1														
<221	> po	lyA_	sign	al												
<222	> 50	55	10													
		1														
<221:																
<222	> 52	/5	38													
<400	> 65										•					
cacte																
	gggc	.ca a	ıggag	taag	c ag	agga	taaa	caa	ctgga	aag	gaga	gcaa	gc a	caaa	igtcat	60
catq	actt	ca c	cato	tqct	c gt	ggaa	acca	aga	taaag	gat	gccc	attt	tc c	acca	gtcat ccaag	120
catq	actt	ca c	cato	tqct	c gt	ggaa	acca	aga atg	taaag ctt	gat gto	gccc acc	attt cag	tc o	acca cta	ccaag gtc	
catq	actt	ca c	cato	tqct	c gt	ggaa	acca	aga atg	taaag ctt Leu	gat gto	gccc acc	attt cag	tc o	acca cta Leu	ccaag gtc Val	120
catg	gctt	ca g	gegte geet	tgct tttt	c gt	ggaa ttgt	acca aagc	aga atç Met	taaaq ctt Leu -35	gat gto Val	gccc acc Thr	attt cag Gln	gga Gly	acca cta Leu -30	ccaag gtc Val	120 174
catge caage	gett cage	ca g	gegte geet	tgct tttt	c gt	ggaa ttgt	acca aagc	aga atg Met	taaaq ctt Leu -35 aga 1	gat gtc Val ttt	gccc acc Thr	cag Gln	tc o gga Gly ttg	acca t cta Leu -30	iccaag igtc iVal ) aaa	120
catge caage	gett cage	ca g	gegte geet tat Tyr	tgct tttt	c gt	ggaa ttgt	acca aagc	aga ato Met tct Ser	taaaq ctt Leu -35	gat gtc Val ttt	gccc acc Thr	cag Gln	tc o gga Gly ttg	acca t cta Leu -30	iccaag igtc iVal ) aaa	120 174
catge caage tac Tyr	gett cage caa Gln gca	ggt Gly	tat Tyr -25	tgct ttt ttg Leu	gca Ala	ggaa ttgt gct Ala ttg	aagc aat Asn	tct Ser -20	taaag ctt Leu -35 aga t Arg l	gat gtc Val ttt Phe ctt	gccc acc Thr gga Gly	cag Gln tca Ser	gga Gly ttg Leu -15	acca Leu -30 ccc Pro	ccaag gtc Val ) aaa Lys	120 174
catge caage tac Tyr	gett cage caa Gln gca	ggt Gly	tat Tyr -25	tgct ttt ttg Leu	gca Ala	ggaa ttgt gct Ala ttg	aagc aat Asn	tct Ser -20	taaag ctt Leu -35 aga t Arg l	gat gtc Val ttt Phe ctt	gccc acc Thr gga Gly	cag Gln tca Ser	gga Gly ttg Leu -15	acca Leu -30 ccc Pro	ccaag gtc Val ) aaa Lys	120 174 222
catgo caago tac Tyr gtt Val	gett cage caa Gln gca Ala	ggt Gly ctt Leu	tat Tyr -25 gct Ala	ttgct tttt ttg Leu ggt Gly	gca Ala ctc Leu	ggaa ttgt gct Ala ttg Leu	aat Aan gga Gly	tct Ser -20 ttt	taaag ctt Leu -35 aga t Arg l	gat gtc Val ttt Phe ctt Leu	gccc acc Thr gga Gly gga Gly	cattt cag Gln tca Ser aag Lys	tc o gga Gly ttg Leu -15 gta Val	acca cta Lev -30 ccc Pro tca	tecaag t gtc t Val ) aaa Lys tac Tyr	120 174 222 270
catgo	gett cage caa Gln gca Ala	ggt Gly ctt Leu	tat Tyr -25 gct Ala	ttgct tttt ttg Leu ggt Gly	gca Ala ctc Leu	ggaa ttgt gct Ala ttg Leu	aat Asn gga Gly -5	aga : ato Met tct Ser -20 ttt Phe	tttt	gat gtc Val ttt Phe ctt Leu	gccc acc Thr gga Gly gga Gly	cattt cag Gln tca Ser aag Lys 1	tc o gga Gly ttg Leu -15 gta Val	tca Ser	tac tyr	120 174 222
catgo	gett cage caa Gln gca Ala	ggt Gly ctt Leu	tat Tyr -25 gct Ala	ttgct tttt ttg Leu ggt Gly	gca Ala ctc Leu	ggaa ttgt gct Ala ttg Leu	aat Asn gga Gly -5	aga : ato Met tct Ser -20 ttt Phe	tttt	gat gtc Val ttt Phe ctt Leu	gccc acc Thr gga Gly gga Gly	cattt cag Gln tca Ser aag Lys 1	tc o gga Gly ttg Leu -15 gta Val	tca Ser	tac tyr	120 174 222 270
catgo	gett cage caa Gln gca Ala	ggt Gly ctt Leu	tat Tyr -25 gct Ala	ttgct tttt ttg Leu ggt Gly	gca Ala ctc Leu	ggaa ttgt gct Ala ttg Leu	aat Asn gga Gly -5	aga : ato Met tct Ser -20 ttt Phe	gctt: Leu -35 aga ! Arg ! ggc Gly ! ttt : Phe	gat gtc Val ttt Phe ctt Leu	gccc acc Thr gga Gly gga Gly	cattt cag Gln tca Ser aag Lys 1	tc o gga Gly ttg Leu -15 gta Val	tca Ser	tac tyr	120 174 222 270 318
catgo	gett cage caa Gln gca Ala gga Gly	ggt Gly ctt Leu -10 gta Val	tat Tyr -25 gct Ala tgc Cys	ttgct ttg Leu ggt Gly cag Gln	gca Ala ctc Leu agt Ser 10	gct Ala ttg Leu aaa Lys	aacca aagc aat Asn gga Gly -5 ttc Phe	aga atc Met tct Ser -20 ttt Phe cat His	ttaaag ctt: Leu -35 aga t Arg l ggc ( Gly ) ttt: Phe	gat gat Val ttt Phe ctt Leu ttte 15 cac	gccc acc Thr gga Gly gga Gly gaa Glu	cattt cag Gln tca Ser aag Lys l gat Asp	tc o gga Gly ttg Leu -15 gta Val cag Gln	acca Leu -30 ccc Pro tca Ser ctc Leu	tac Tyr cgt Arg 20 tgt	120 174 222 270
catgo	gett cage caa Gln gca Ala gga Gly	ggt Gly ctt Leu -10 gta Val	tat Tyr -25 gct Ala tgc Cys	ttgct ttg Leu ggt Gly cag Gln	gca Ala ctc Leu agt Ser 10	gct Ala ttg Leu aaa Lys	aacca aagc aat Asn gga Gly -5 ttc Phe	aga atc Met tct Ser -20 ttt Phe cat His	ttaaag ctt: Leu -35 aga t Arg l ggc ( Gly ) ttt: Phe	gat gat Val ttt Phe ctt Leu ttte 15 cac	gccc acc Thr gga Gly gga Gly gaa Glu	cattt cag Gln tca Ser aag Lys l gat Asp	tc o gga Gly ttg Leu -15 gta Val cag Gln	acca Leu -30 ccc Pro tca Ser ctc Leu	tac Tyr cgt Arg 20 tgt	120 174 222 270 318
catge caage tac Tyr gtt Val ata Ile 5 ggg Gly	gett cage caa Gln gca Ala gga Gly gct Ala	ggt Gly ctt Leu -10 gta Val	tat Tyr -25 gct Ala tgc Cys	ttgct tttt ttg Leu ggt Gly cag Gln ggt Gly 25	gca Ala ctc Leu agt Ser 10 cca Pro	gct Ala ttg Leu aaa Lys cag	aacca aagc aat Asn gga Gly -5 ttc Phe cat	aga atc Met tct Ser -20 ttt Phe cat His aac	gctt: Leu -35 aga t Arg l ggc Gly l ttt Phe agg Arg 30	gat gtc Val ttt Phe ctt Leu ttt Phe 15 cac	gccc acc Thr gga Gly gga Gly gaa Glu tgc Cys	cattt cag Gln tca Ser aag Lys l gat Asp	tc c gga Gly ttg Leu -15 gta Val cag Gln ctt Leu	tca Ser Ctc Leu acc Thr	tac Tyr cgt Arg 20 tgt Cys	120 174 222 270 318
catge caage tac Tyr gtt Val ata Ile 5 ggg Gly	gett cage caa Gln gca Ala gga Gly gct Ala	ggt Gly ctt Leu -10 gta Val	tat Tyr -25 gct Ala tgc Cys	ttgct tttg Leu ggt Gly cag Gln ggt Gly 25 ata	gca Ala ctc Leu agt Ser 10 cca Pro	ggaa ttgt gct Ala ttg Leu aaa Lys cag Gln	aat Asn Gly -5 ttc Phe cat His	aga atc Met tct Ser -20 ttt Phe cat His aac Asn	gctt: Leu -35 aga 1 Arg 1 ggc Gly 1 ttt Phe agg Arg 30 agt	gat	gccc acc Thr gga Gly gga Gly gaa Glu tgc Cys	cattt cag Gln tca Ser aag Lys l gat Asp ctc Leu	tc c gga Gly ttg Leu -15 gta Val cag Gln ctt Leu	tca ser ctc tca ser ctc Leu acc Thr	tac Tyr cgt Arg 20 tgt Cys cag	120 174 222 270 318
catge caage tac Tyr gtt Val ata Ile 5 ggg Gly	gett cage caa Gln gca Ala gga Gly gct Ala	ggt Gly ctt Leu -10 gta Val	tat Tyr -25 gct Ala tgc Cys	ttgct tttg Leu ggt Gly cag Gln ggt Gly 25 ata	gca Ala ctc Leu agt Ser 10 cca Pro	ggaa ttgt gct Ala ttg Leu aaa Lys cag Gln	aat Asn Gly -5 ttc Phe cat His	aga atc Met tct Ser -20 ttt Phe cat His aac Asn	gctt: Leu -35 aga 1 Arg 1 ggc Gly 1 ttt Phe agg Arg 30 agt	gat	gccc acc Thr gga Gly gga Gly gaa Glu tgc Cys	cattt cag Gln tca Ser aag Lys l gat Asp ctc Leu	tc c gga Gly ttg Leu -15. gta Val cag Gln ctt Leu gac Asp	tca ser ctc tca ser ctc Leu acc Thr	tac Tyr cgt Arg 20 tgt Cys cag	120 174 222 270 318
catge caage tac Tyr gtt Val ata Ile 5 999 Gly gag Glu	gett cage caa Gln gca Ala gga Gly gct Ala gaa Glu	ggt Gly ctt Leu -10 gta Val ggt Gly tgc Cys	tat Tyr -25 gct Ala tgc Cys ttt Phe aaa Lys	ttgct tttg Leu ggt Gly cag Gln ggt Gly 25 ata Ile	gca Ala ctc Leu agt Ser 10 cca Pro aag Lys	ggt gct Ala ttg Leu aaa Lys cag Gln cat	aat Asn gga Gly -5 ttc Phe cat His	aga: atc Met tct Ser -20 ttt Phe cat His aac Asn tta Leu 45	gctt: Leu -35 aga 1 Arg 1 ggc Gly 1 ttt Phe agg Arg 30 agt Ser	gat gat gat val ttt Phe ctt ttt Phe cac His gag Glu	gccc : accc : Thr gga Gly gga Gly tgc Cys aag Lys	cattt cag Gln tca Ser aag Lys l gat Asp ctc Leu gga Gly	tc c gga Gl ₃ ttg Leu -15. gta Val cag Gln ctt Leu gac Asp 50	acca cta ccc Pro tca Ser ctc Leu acc Thr 35 tct	tac Tyr cgt Arg 20 tgt Cys cag Gln	120 174 222 270 318 366
catge caage tac Tyr gtt Val ata Ile 5 999 Gly gag Glu	gett cage caa Gln gca Ala gga Gly gct Ala gaa Glu	ggt Gly ctt Leu -10 gta Val ggt Gly tgc Cys	tat Tyr -25 gct Ala tgc Cys ttt Phe aaa Lys	ttgct tttg Leu ggt Gly cag Gln ggt Gly 25 ata Ile	gca Ala ctc Leu agt Ser 10 cca Pro aag Lys	ggt gct Ala ttg Leu aaa Lys cag Gln cat	aat Asn gga Gly -5 ttc Phe cat His	aga: atc Met tct Ser -20 ttt Phe cat His aac Asn tta Leu 45	gctt: Leu -35 aga 1 Arg 1 ggc Gly 1 ttt Phe agg Arg 30 agt	gat gat gat val ttt Phe ctt ttt Phe cac His gag Glu	gccc : accc : Thr gga Gly gga Gly tgc Cys aag Lys	cattt cag Gln tca Ser aag Lys l gat Asp ctc Leu gga Gly	tc c gga Gl ₃ ttg Leu -15. gta Val cag Gln ctt Leu gac Asp 50	acca cta ccc Pro tca Ser ctc Leu acc Thr 35 tct	tac Tyr cgt Arg 20 tgt Cys cag Gln	120 174 222 270 318
catge caage tac Tyr gtt Val ata Ile 5 ggg Gly gag Glu	gettecage caac Gln gea Ala Gly get Ala Glu tca	ca ggt ggt gly ctt Leu -10 gta Val ggt Gly tgc Cys	tat Tyr -25 gct Ala tgc Cys ttt Phe aaa Lys	ttgct tttg Leu ggt Gly cag Gln ggt Gly 25 ata Ile	gca Ala ctc Leu agt Ser 10 cca Pro aag Lys	ggt gct Ala ttg Leu aaa Lys cag Gln cat	aat Asn gga Gly -5 ttc Phe cat His	aga: atc Met tct Ser -20 ttt Phe cat His aac Asn tta Leu 45	gctt: Leu -35 aga 1 Arg 1 ggc Gly 1 ttt Phe agg Arg 30 agt Ser	gat gat gat val ttt Phe ctt ttt Phe cac His gag Glu	gccc : accc : Thr gga Gly gga Gly tgc Cys aag Lys	cattt cag Gln tca Ser aag Lys l gat Asp ctc Leu gga Gly	tc c gga Gl ₃ ttg Leu -15. gta Val cag Gln ctt Leu gac Asp 50	acca cta ccc Pro tca Ser ctc Leu acc Thr 35 tct	tac Tyr cgt Arg 20 tgt Cys cag Gln	120 174 222 270 318 366
catge caage tac Tyr gtt Val ata Ile 5 999 Gly gag Glu cct Pro	gett cage caa Gln gca Ala gga Gly gct Ala gaa Glu tca Ser	ca ggt Gly ctt Leu -10 gta Val ggt Gly tgc Cys gct Ala	tat Tyr -25 gct Ala tgc Cys ttt Phe aaa Lys 40 tcc Ser	ttgct tttg Leu ggt Gly cag Gln ggt Gly 25 ata Ile	gca Ala ctc Leu agt Ser 10 cca Pro aag Lys	ggt Ala ttg Leu aaa Lys cag Gln cat His	aat Asn gga Gly -5 ttc Phe cat His gga Gly	aga: atc Met tct Ser -20 ttt Phe cat His aac Asn tta 45 gtga	gctt: Leu -35 aga 1 Arg 1 ggc Gly 1 ttt Phe agg Arg 30 agt Ser ct tt	gat gat yal ttt Phe ctt Leu ttt Phe sqag Glu cga	gccc : acc : Thr gga Gly gga Glu tgc Cys aag Lys	cattt cag Gln tca Ser aag Lys l gat Asp ctc Leu gga Gly t ttt	tc c gga Gl _y ttg Leu -15. gta Val cag Gln ctt Leu gac Asp 50 caaaa	acca cta ccc Pro tca Ser ctc Leu acc Thr 35 tct Ser	tac Tyr cgt Arg 20 tgt Cys cag Gln	120 174 222 270 318 366 414
catge caage tac Tyr gtt Val ata Ile 5 999 Gly gag Glu cct Pro	gettecage caac Gln gea Ala gga Gly get Ala gaa Glu tca Ser	ca control of the con	tat Tyr -25 gct Ala tgc Cys ttt Phe aaa Lys 40 tcc Ser	ttgct tttg Leu ggt Gly cag Gln ggt Gly 25 ata Ile	gca Ala ctc Leu agt Ser 10 cca Pro aag Lys	ggt Ala ttg Leu aaa Lys cag Gln cat His	aat Asn gga Gly -5 ttc Phe cat His gga Gly	aga: atc Met tct Ser -20 ttt Phe cat His aac Asn tta 45 gtga	gctt: Leu -35 aga 1 Arg 1 ggc Gly 1 ttt Phe agg Arg 30 agt Ser ct tt	gat gat yal ttt Phe ctt Leu ttt Phe sqag Glu cga	gccc : acc : Thr gga Gly gga Glu tgc Cys aag Lys	cattt cag Gln tca Ser aag Lys l gat Asp ctc Leu gga Gly t ttt	tc c gga Gl _y ttg Leu -15. gta Val cag Gln ctt Leu gac Asp 50 caaaa	acca cta ccc Pro tca Ser ctc Leu acc Thr 35 tct Ser	tac Tyr cgt Arg 20 tgt Cys cag Gln	120 174 222 270 318 366 414

<210> 66 <211> 1747

<212> DNA

<213 > Homo sapiens

<220>

WO 99/31236 -43- PCT/IB98/02122

<221> CDS <222> 10..1062 <221> sig_peptide <222> 10..57 <223> Von Heijne matrix score 4.9 seq FIYLQAHFTLCSG/WS <221> polyA_signal <222> 1710..1715 <221> polyA_site <222> 1735..1747 <400> 66 geoteacca atg gtt coc tto atc tat ctg caa gcc cac ttt aca ctc tgt Met Val Pro Phe Ile Tyr Leu Gln Ala His Phe Thr Leu Cys 99 tot ggg tgg tcc agc aca tac cgg gac ctc cgg aag ggt gtg tat gtg Ser Gly Trp Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val 5 ccc tac acc cag ggc aag tgg gaa ggg gag ctg ggc acc gac ctg gta 147 Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val 25 20 age ate eee cat gge eee aac gte act gtg egt gee aac att get gee 195 Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala 40 atc act gaa tca gac aag ttc ttc atc aac ggc tcc aac tgg gaa ggc 243 Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly 55 atc ctg ggg ctg gcc tat gct gag att gcc agg cct gac gac tcc ccg 291 Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Pro 70 gag cct ttc ttt gac tct ctg gta aag cag acc cac gtt ccc aac ctc 339 Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu 85 tto too otg cag ott tgt ggt got ggo tto occ otc aac cag tot gaa 387 Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu 105 100 gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc gac cac Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His 120 115 teg etg tac aca gge agt etc tgg tat aca eec atc egg egg gag tgg 483 Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp 135 531 tat tat gag gtg atc att gtg cgg gtg gag atc aat gga cag gat ctg Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu 150 145 579 aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg gac agt Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser 170 165 ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct gca gtc 627 Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val 185 180 175 aaa too ato aag goa goo too too acg gag aag tto cot gac ggt tto 675 Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe 200 205 723 tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc cct tgg Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp 215 220 210 aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt acc aac 771

Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn 225 230 235	
cag too tto ogo ato aco ato ott cog cag caa tac otg ogg coa gtg Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val	819
240 245 250	867
gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc atc tca Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser	
255 260 265 270	
cag toa too acg gge act gtt atg gga get gtt atc atg gag gge tte	915
Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe 275 280 285	
tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct gtc agc	963
Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser	
290 295 300	
gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa ggc ccn Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro	
305 310 315	
ttt tgt cac ctt gga cat gga aga ctg tgg cta caa cat tcc aca gac	1059
Phe Cys His Leu Gly His Gly Arg Leu Trp Leu Gln His Ser Thr Asp	,
320 325 330 aga tgagtcaacc ctcatgacca tagcctatgt catggctgcc atctgcgccc	1112
Arg	
335	
tottcatgot gocactotgo otcatggtgt gtcagtggcg otgoctcogo tgcctgcg	gcc 1172 cag 1232
agcagcatga tgactttgct gatgacatct ccctgctgaa gtgaggaggc ccatgggc aagataggga ttcccctgga ccacacctcc gtggttcact ttggtcacaa gtaggaga	
cagatogoac ctotogocaq agcaceteag gaceeteece acceaceaaa tgeeteeg	366 1352
ttgatggaga aggaaaaggc tggcaaggtg ggttccaggg actgtacctg taggagac	cag 1412
aaaagagaag aaagaagcac tetgetggeg ggaatactet tggteacete aaatttaa	agt 14/2
cgggaaattc tgctgcttga aacttcagcc ctgaaccttt gtcaccattc ctttaaat tccaacccaa agtattcttc ttttcttagt ttcagaagta ctggcatcac acgcaggt	
cettogegto totecetoto otaccetoge agagaagaga ceaagettot ticeeto	ctg 1632
gccaaagtca gtaggagagg atgcacagtt tgctatttgc tttagagaca gggactg	Lac 1/12
aaacaagcct aacattggtg caaaaaaaaa aaaaa	1747

<211> 1686

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 78..491

<221> sig_peptide

<222> 78..218

<223> Von Heijne matrix
 score 5.8
 seq LMCFGALIGLCAC/IC

<221> polyA_signal

<222> 1652..1657

<221> polyA_site

<222> 1673..1686

c400> 67
ggtatagccc accagaaagg acagagtcat ttgatgtggt cacaaaatgt gtgagtttca 60
cactaactga gcagttc atg gag aaa ttt gtt gat ccc gga aac cac aat 110
Met Glu Lys Phe Val Asp Pro Gly Asn His Asn

	-45		-40	
age ggg att gat c	tc ctt agg acc	tat ctt tgg	cgt tgc cag tt	c ctt 158
Ser Gly Ile Asp Lo	eu Leu Arg Thr	Tyr Leu Trp	Arg Cys Gln Ph	ie Leu
-35	-30		-25	
tta cct ttt gtg ag	gt tta ggt ttg	atg tgc ttt	ggg gct ttg at	cgga 206
Leu Pro Phe Val Se	er Leu Gly Leu	Met Cys Phe	Gly Ala Leu Il	e Gly
-20	-15	-10		-5
ctt tgt gct tgc a				
Leu Cys Ala Cys I	le Cys Arg Ser	Leu Tyr Pro		ir Gly
1		5	10	
att ctc cat ctc c				
Ile Leu His Leu L		Cys Thr Leu		er Cys
15	20		25	et gac 350
tat gtt gct gga a				- 3
Tyr Val Ala Gly I			Leu Glu Leu Pi 40	o wab
30	35			c tot 398
aat gta tcc ggt g Asn Val Ser Gly G				
45	50	55	Ded Ala Cys V	60
gct ccc tta cag t			atc too oct o	
Ala Pro Leu Gln P	he Met Ala Ser	Ala Leu Phe	Ile Tro Ala A	la His
6		70	7:	
acc aac cgg aga g	-	atg aag gca	tat cqt qtq g	ca 491
Thr Asn Arg Arg G	lu Tvr Thr Leu	Met Lys Ala	Tyr Arg Val A	la
80		85	90	
tgagcaagaa actgcc	tgct ttacaattg	c catttttatt	tttttaaaat aa	tactgata 551
ttttccccac ctctca	attg tttttaatt	t ttatttgtgg	atataccatt tt	attatg <b>a</b> a 611
aatctatttt atttat	acac attcaccac	t aaatacacac	ttaataccac ta	aaatttat 671
gtggtttact ttaagc	gatg ccatctttc	a aataaactaa	tctaggtcta ga	cagaaaga 731
aatggataga gacttg	acac aaatttatg	a aagaaaattg	ggagtaggaa tg	tgaccgaa 791
aacaagttgt gctaat	gtct gttagactt	t tcagtaaaac	caaagtaact gt	atctgttc 851
aactaaaaac tctata	ttag tttctttgg	g aaacctctca	tcgtcaaaac tt	tatgttca 911
ctttgctgtt gtagat	agcc agtcaacca	g cagtattagt	gctgttttca aa	gatttaag 971
ctctataaaa ttggga	aatt atctaagat	c attttcccta	agcattgaca ca	tagettea 1031
tctgaggtga gatatg	gcag ctgtttgta	t ctgcactgtg	totgtotaca aa	gagtgaaa 1091 ggccgggc 1151
aatacagtgt ttactt	gaaa ttttaactt	t gtaactgcaa	gaattccagt to	3300333
gaggattagt attatt	ttta actctccgt	a agattttcag	taccaccaaa tt	5000055
tttttttttt ttct	ttca cataccagg	g ttattaaaag	tgtgetttet tt	
tattacagtt acaagg	taaa attootoaa	c tgctatttat	ttattccage co	
aaagaacgtt tcacca	taat gaccctcca	g agetgggaaa	cetaceacaa ga	
tctggctgtc cattaa	cctc caactatgg	cettattet	trateret c	
ttccttgcct aaatco	cttc ctggtgtgt	a tcaacattat	aschtatte th	
cattttttat aagtat	gtet ataaacatt	g additidada	atttcttacc at	
tactgtagca attgac	agat taaaaaaat	e asserted	Cassassas as	
tgtcttttt aaaaaa	itaaa attaaaaat	y aaaayayacc	Cadaaaaaa a	1000

<211> 542

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 69..371

<221> sig_peptide <222> 69..287

<223> Von Heijne matrix score 4

seq AVGFLFWVIVLTS/WI

<221> polyA_signal <222> 510515	
<221> polyA_site <222> 530542	
<400> 68 tgttacttag ggtcaagget tgggtettge eeegcaaace ettgggaega eeeggeeeea gegeaget atg aac etg gag ega gtg tee aat gag gag aaa ttg aac etg Met Asn Leu Glu Arg Val Ser Asn Glu Glu Lys Leu Asn Leu -70 -65	60 110
tgc cgg aag tac tac ctg ggg ggg ttt gct ttc ttg cct ttt ctc tgg Cys Arg Lys Tyr Tyr Leu Gly Gly Phe Ala Phe Leu Pro Phe Leu Trp -50 -45	158
ttg gtc aac atc ttc tgg ttc tac cga gag gcc ttc ctt gtc cca gcc Leu Val Asn Tle Phe Trp Phe Tym Arg Glu Ala Phe Leu Val Pro Ala -40 -35 -30	206
tac aca gaa cag agc caa atc aaa ggc tat gtc tgg cgc tca gct gtg Tyr Thr Glu Gln Ser Gln Ile Lys Gly Tyr Val Trp Arg Ser Ala Val	254
ggo tto oto tto tgg gtg ata gtg oto aco too tgg ato aco ato tto Gly Phe Leu Phe Trp Val Ile Val Leu Thr Ser Trp Ile Thr Ile Phe	302
cag atc tac cgg ccc cgc tgg ggt gcc ctt ggg gac tac ctc tcc ttc Gln Ile Tyr Arg Pro Arg Trp Gly Ala Leu Gly Asp Tyr Leu Ser Phe	350
10 15 20 acc ata ccc ctg ggc acc ccc tgacaacttc tgcacatact ggggccctgc Thr Ile Pro Leu Gly Thr Pro	401
25 ttattetece aggacagget cettaaagea gaggageetg teetgggage ceetteteaa acteetaaga ettgttetea tgteecaegt tetetgetga cateeceaa taaaggacee taaettteaa aaaaaaaaaa a	461 521 542
<210> 69 <211> 1174 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 2757	
<221> sig_peptide <222> 2205 <223> Von Heijne matrix score 7.3 seq LRLILSPLPGAQP/QQ	
<221> polyA_site   <222> 11601174	
<pre>&lt;400&gt; 69 g atg cct gag ggc ccc gag ctg cac ctg gcc agc cag ttt gtg aat gag Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu -65 -60 -55</pre>	4
gcc tgc agg gcg ctg gtg ttc ggc ggc tgc gtg gag aag tcc tct gtc Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val	9
age ege aac eet gag gtg eec ttt gag age agt gee tae ege ate tea	14

	Arg					-30					-25					
act	tca	acc	cac	aac	aaq	gag	ctq	cgc	ctg	ata	ctg	agc	cct	ctg	cct	193
Δla	Ser	Ala	Arg	Glv	Lvs	Glu	Leu	Arg	Leu	Ile	Leu	Ser	Pro	Leu	Pro	
-20			3		-15			-		-10					-5	
720	gcc	cad	cct	caa		gag	cca	cta	acc	ctq	qtc	ttc	cgc	ttc	ggc	241
999	Ala	Cla	Dro	Gln	Cla	Glu	Dro	Len	Ala	Leu	Val	Phe	Arq	Phe	Glv	
GIÀ	Ald	GIII	110	1	GIII	GIU	110	5				•	10			
	tcc			1	~~~	ata	ata		cac	gag	aaa	cta		cac	cat	289
atg	tee	ggc	100	25-	Cay	Tan	919	Dra	720	Glu	Glu	Len	Pro	Ara	His	
Met	Ser		ser	Pne	GIR	Leu		PIO	Arg	GIU	GIU	25		3		
		15					20						a= a	acc	cta	337
gcc	cac	ctg	cgc	ttt	tac	acg	acc	ccg	CCT	ggc	Des	299	Tou	31 a	Leu	,,,
Ala	His	Leu	Arg	Phe	Tyr		Ala	Pro	Pro	GIY	Pro	Arg	pen	Ala	Dea	
	30	٠				35					40					205
tgt	ttc	gtg	gac	atc	cgc	cgg	ttc	ggc	cgc	tgg	gac	ctt	āāā	gga	aag	385
Сув	Phe	Val	Asp	Ile	Arg	Arg	Phe	Gly	Arg	Trp	Asp	Leu	GIA	GIA	гав	
45					50					55					60	
Faa	cag	cca	qqc	cqc	qqq	CCC	tgt	gtc	ttg	cag	gag	tac	cag	cag	ttc	433
	Gln	Pro	Glv	Ara	Glv	Pro	Cys	Val	Leu	Gln	Glu	Tyr	Gln	Gln	Phe	
115	01		1	65	1		•		70					75		
	gag	22 <b>+</b>	ata	cta	cga	aac	cta	aca	gat	aaq	qcc	ttt	gac	cgg	ccc	481
499	Glu	200	203	Leu	220	Acn	Len	Ala	Asp	Lvs	Ala	Phe	Asp	Arg	Pro	
Arg	GIU	Wali		Deu	n. a	AD II	204	85		-1-			90	_		
			80			~~~	C 3 C		ttc	ttc	aat	ggc	att	aac	aac	529
atc	tgc	gag	gcc	CEC	ctg	gac	Cay	299	Dhe	Dhe	Δαπ	Glv	Tle	Glv	Asn	
Ile	Cys		Ala	Leu	Leu	Asp	GIR	Arg	PILE	FILE	Man	105	110	<b>U</b> _1	Asn	
		95					100								G2G	577
tat	ctg	cgg	gca	gag	atc	ctg	tac	cgg	ctg	aag	acc	7	200	Dha	gag	3,,,
Tyr	Leu	Arg	Ala	Glu	Ile			Arg	Leu	rAa	116	PIO	PIO	PILE	Glu	
	110					115					120					625
aag	gcc	cgc	tcg	gtc	ctg	gag	gcc	ctg	cag	cag	cac	: agg	cca	ago	ccg	025
Lys	Ala	Arg	Ser	Val	Leu	Glu	Ala	Leu	Gļņ	Glr	His	Arg	Pro	ser	Pro	
125					130					135	•				140	
gag	cta	acc	ctq	ago	cag	aag	ata	agg	acc	aac	cts	g cag	, aat	tca	gac	673
Glu	Leu	Thr	Leu	Ser	Gln	Lys	Ile	Arg	Thr	Lys	Lei	ı Glr	l Asn	Ser	Asp	
				145					150	)				122	•	
cto	cta	gag	cta	tat	cac	tca	ata	ccc	aag	gaa	gt	ggto	cag	ttg	ggt	721
Len	Len	6)11	T.e.	CVA	His	Ser	Val	Pro	Lys	Glı	ı Va	l Val	Glr	Let	ı Gly	
пеп	. Deu	GIG	160			•		169	;			-	170	)		
	gcc		100		200	. 220	cto			age	aa:	a tga	attqt	gta		767
gag	Ala	dad	gat	990	. cov	. Acr	LAI	CV	Dh	Set	r Lv	8	_	-		
GIU	Ala			, Ст	361	YOI	180	. 0, .			,	_				
		175							.++.		a ++	taga	agtt	tata	acccta	827
acc	ctgg	ggc	actt	gtco	cc c	CCE	gacc	it ga		accy.	a cc	-	2300	cto	ageceta	887
gct	gata	ctc	aato	gact	ag g	CCE	CCCC	10 01	igic	adid	y	~~~		200	ggcgcag	947
tgg	jctca	tgc	ctgt	ggt	cc s	gca	CCCC	39. 9°	aggc	cgag	· 99	9919	9000	200	tgaggtc	1007
300	-aa+	C03	7200	atco	ta c	ccaa	acato	ia to	gaaa	cccc	а сс	tcca	ctaa	dat	ycaaaaa	1067
att	adec	agg	tate	ata	ica (	acao	cctq	ta gʻ	CCCC	agct	a ct	cggg	agga	cya	ggcagga	1127
aaa	tcac	tta	aaco	cago	ag c	ataga	aggti	tg c	agtt	gagc	t ga	gatc	gtgc	cat	tgcactc	
cac	cct	ggc	aaco	gaga	gca a	aaac	tcca	tc t	caaa	aaaa	a aa	aaaa	a			1174
					_											

<211> 1285

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 2..1051

<221> sig_peptide <222> 2..205

WO 99/31236 -48- PCT/IB98/02122

<223> Von Heijne matrix score 7.3 seq LRLILSPLPGAQP/QQ <221> polyA_signal <222> 1248..1253 <221> polyA_site <222> 1272..1285 <400> 70 g atg cet gag gge eee gag etg eac etg gee age eag tit gtg aat gag Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu -65 -60 gcc tgc agg gcg ctg gtg ttc ggc ggc tgc gtg gag aag tcc tct gtc 97 Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val -45 age ege aac eet gag gtg eec ttt gag age agt gee tac ege ate tea 145 Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser -30 get tea gee ege gge aag gag etg ege etg ata etg age eet etg eet 193 Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro -15 ggg gcc cag ccc caa cag gag cca ctg gcc ctg gtc ttc cgc ttc ggc 241 Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly 289 atg tcc ggc tct ttt cag ctg gtg ccc cgc gag gag ctg cca cgc cat Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His 25 20 gee eac etg ege tit tae aeg gee eeg eet gge eec egg ete gee eta 337 Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu 35 tgt ttc gtg gac atc cgc cgg ttc ggc cgc tgg gac ctt ggg gga aag 385 Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys 50 55 tgg cag ccg ggc cgc ggg ccc tgt gtc ttg cag gag tac cag cag ttc 433 Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe agg ctg aag atc ccc ccc ttt gag aag gcc cgc tcg gtc ctg gag gcc Arg Leu Lys Ile Pro Pro Phe Glu Lys Ala Arg Ser Val Leu Glu Ala . 85 80 ctg cag cag cac agg ccg agc ccg gag ctg acc ctg agc cag aag ata 529 Leu Gln Gln His Arg Pro Ser Pro Glu Leu Thr Leu Ser Gln Lys Ile 100 agg acc aag ctg cag aat cca gac ctg ctg gag cta tgt cac tca gtg Arg Thr Lys Leu Gln Asn Pro Asp Leu Leu Glu Leu Cys His Ser Val 115 625 ccc aag gaa gtg gac cag ttg ggg ggc agg ggc tac ggg tca gag agc Pro Lys Glu Val Asp Gln Leu Gly Gly Arg Gly Tyr Gly Ser Glu Ser 130 135 125 673 ggg gag gag gac ttt gct gcc ttt cga gcc tgg ctg cgc tgc tat ggc Gly Glu Glu Asp Phe Ala Ala Phe Arg Ala Trp Leu Arg Cys Tyr Gly 721 atg cca ggc atg agc tcc ctg cag gac cgg cat ggc cgt acc atc tgg Met Pro Gly Met Ser Ser Leu Gln Asp Arg His Gly Arg Thr Ile Trp 165 160 ttc cag ggg gat cct gga ccg ttg gca ccc aaa ggg cgc aag tcc cgc 769 Phe Gln Gly Asp Pro Gly Pro Leu Ala Pro Lys Gly Arg Lys Ser Arg 185 180 175 817 aaa aag aaa too aag goo aca cag otg agt oot gag gac aga gtg gag Lys Lys Lys Ser Lys Ala Thr Gln Leu Ser Pro Glu Asp Arg Val Glu 200 195 190

WO 99/31236 -49- PCT/IB98/02122

gac gct ttg cct cca agc aag gcc cct tcc aag aca cga agg gca aag Asp Ala Leu Pro Pro Ser Lys Ala Pro Ser Lys Thr Arg Arg Ala Lys 205 210 215 220	865
aga gac ctt cct aag agg act gca acc cag cgg cct gag ggg acc agc Arg Asp Leu Pro Lys Arg Thr Ala Thr Gln Arg Pro Glu Gly Thr Ser 225 230 235	913
Ctc cag cag gac cca gaa gct ccc aca gtg ccc aag aag ggg agg agg Leu Gln Gln Asp Pro Glu Ala Pro Thr Val Pro Lys Lys Gly Arg Arg	961
aag ggg cga cag gca gcc tct ggc cac tgc aga ccc cgg aag gtc aag Lys Gly Arg Gln Ala Ala Ser Gly His Cys Arg Pro Arg Lys Val Lys 255 260 265	1009
gct gac atc cca tcc ttg gaa cca gag ggg acc tca gcc tct Ala Asp Ile Pro Ser Leu Glu Pro Glu Gly Thr Ser Ala Ser 270 280	1051
taggagg ctctccttgc ttgcactcac cctttcttat tgtcttgccc tgcatctggg	1111
ggtotgaatt tttgggagga gggaatatot qaaqqtqcaa acaggcccta cggctgttcc	1171
ctgcacact ctratggttt taattgtacc ccatcttcca catctttaaa gcttatytya	1231
aaaatgctgc atttttaata aactgataca tttgaactcc aaaaaaaaaa	1285
<pre>&lt;210&gt; 71 &lt;211&gt; 1398 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 21171  &lt;221&gt; sig_peptide &lt;222&gt; 2205 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;400&gt; 71 g atg cct gag ggc ccc gag ctg cac ctg gcc agc cag ttt gtg aat gag Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu -60 -55</pre>	49
gcc tgc agg gcg ctg gtg ttc ggc ggc tgc gtg gag aag tcc tct gtc Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val	97
agc cgc aac cct gag gtg ccc ttt gag agc agt gcc tac cgc atc tca Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser	145
gct tca gcc cgc ggc aag gag ctg cgc ctg ata ctg agc cct ctg cct Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro -20 -15 -10 -5	
ggg gcc cag ccc caa cag gag cca ctg gcc ctg gtc ttc cgc ttc ggc Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly 1 5 10	241
ate too age tot tit cag ctg gtg ccc cgc gag gag ctg cca cgc cat	289
Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His  20 25	

WO 99/31236 -50- PCT/IB98/02122

gcc Ala	cac His	ctg Leu	cgc Arg	ttt Phe	tac Tyr	acg Thr	gcc Ala	ccg Pro	cct Pro	ggc Gly	ccc Pro	cgg Arg	ctc Leu	gcc Ala	cta Leu	337
tat	30 ttc	ara	gac	atc	cac	35 cgg	ttc	aac	cac	taa	40 gac	ctt	aaa	gga	aad	385
Cys 45	Phe	Val	Asp	Ile	Arg 50	Arg	Phe	Gly	Arg	Trp 55	Asp	Leu	Gly	Gly	Lys 60	303
tgg	cag	ccg	ggc	cgc	999	ccc	tgt	qtc	ttg	cag	gag	tac	caq	caq	ttc	433
	_	_			-	Pro	-	-	_	_			_	_		
						aac										481
			80			Asn		85					90			
	_		_		_	gac	_									529
		95				Asp	100					105				
						ctg										577
	110					Leu 115					120					
						gag										625
Lys 125	Ala	Arg	ser	Val	130	Glu	Ala	Leu	GIN	135	HIS	Arg	Pro	ser	Pro 140	
	a+ <b>a</b>	200		200		aag	2+2	200	300		ata		225	003		673
						Lys										673
014	Dea	1111	Deu	145	OI.	בעם	110	AL 9	150	Lys	Dea	<b>J</b> 1.1	A311	155	nop	
cta	cta	gag	cta		cac	tca	ata	ccc		gaa	ata	atc	caq		aga	721
_	_			_		Ser			-	_		-	-,	-		
			160	•				165	•				170		•	
ggc	aga	ggc	tac	999	tca	gag	agc	<b>9</b> 99	gag	gag	gac	ttt	gct	gcc	ttt	769
						Glu										
cga	gcc	tgg	ctg	cgc	tgc	tat	ggć	atg	cca	ggc	atg	agc	tcc	ctg	cag	817
						Tyr 195										
						atc										865
	Arg	His	Gly	Arg		Ile	Trp	Phe	Gln		Asp	Pro	Gly	Pro		
205					210					215					220	017
						tcc										913
				225		Ser			230					235		961
						gtg										901
Leu	ser	Pro	240	Asp	Arg	Val	GIU	245	Ala	Leu	PIO	PIO	250	пåа	ALG	
cct	tcc	add		cga	acid	gca	аад		gac	ctt	cct	aag		act	gca	1009
						Ala										
		255			5		260					265	5			
acc	cag	cgg	cct	gag	999	acc	agc	ctc	cag	cag	gac	cca	gaa	gct	CCC	1057
												Pro			Pro	
															ggc	1105
Thr	Val	Pro	Lys	Lys	Gly	Arg	Arg	Lys	Gly	Arg	Gln	Ala	Ala	Ser	Gly	
285			-	_	290					295					300	
															cca	1153
His	Cys	Arg	Pro	Arg 305	Lys	Val	Lys	Ala	Asp 310		Pro	Ser	Leu	Glu 315	Pro	
						tag	cagg	agg	ctct	cctt	gc t	tgca	ctca	C		1201
Glu	Gly	Thr	Ser 320	Ala	Ser											
															atatct	1261
gaag	ggtg	caa a	acag	gccc	ta c	ggct	gttc	c ct	gcac	aact	ctc	atgg	jttt	taat	tgtacc	1321
ccat	ctt	cca (	catc	ttta	aa g	ctca	tgtg	a aa	aatg	ctgo	att	ttta	ata	aact	gataca	1381
ttt	gaaa	aaa	aaaa	aaa												1398

WO 99/31236 -51- PCT/IB98/02122

```
<210> 72
<211> 821
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 42..611
<221> sig_peptide
<222> 42..287
<223> Von Heijne matrix
     score 4.4
      seq NLPHLQVVGLTWG/HI
<221> polyA_signal
<222> 787..792
<221> polyA_site
<222> 808..821
cogttgccag ttctgcgcgt gtcctgcgtc tccagtatgg a atg tat gtt tgg ccc
                                              Met Tyr Val Trp Pro
tgt gct gtg gtc ctg gcc cag tac ctt tgg ttt cac aga aga tct ctg
                                                                     104
Cys Ala Val Val Leu Ala Gln Tyr Leu Trp Phe His Arg Arg Ser Leu
                            -70
                                                -65
cca ggc aag gcc atc tta gag att gga gca gga gtg agc ctt cca gga
                                                                     152
Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala Gly Val Ser Leu Pro Gly
    -60
                        -55
att ttg act gcc aaa tgt ggt gca gaa gta ata ctg tca gac agc tca
                                                                     200
Ile Leu Thr Ala Lys Cys Gly Ala Glu Val Ile Leu Ser Asp Ser Ser
                    -40
                                        -35
gaa ctg cct cac tgt ctg gaa gtc tgt cgg caa agc tgc caa atg aat
                                                                     248
Glu Leu Pro His Cys Leu Glu Val Cys Arg Gln Ser Cys Gln Met Asn
                -25
                                    -20
                                                                      296
aac ctg cca cat ctg cag gtg gta gga cta aca tgg ggt cat ata tct
Asn Leu Pro His Leu Gln Val Val Gly Leu Thr Trp Gly His Ile Ser
                                - 5
            -10
tgg gat ctt ctg gct cta cca cca caa gat att atc ctt gca tct gat
                                                                      344
Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp Ile Ile Leu Ala Ser Asp
                                            15
                        10
gtg ttc ttt gaa cca gaa gat ttt gaa gac att ttg gct aca ata tat
                                                                      392
Val Phe Phe Glu Pro Glu Asp Phe Glu Asp Ile Leu Ala Thr Ile Tyr
                                        30
                    25
ttt ttg atg cac aag aat ccc aag gtc caa ttg tgg tct act tat caa
                                                                      440
Phe Leu Met His Lys Asn Pro Lys Val Gln Leu Trp Ser Thr Tyr Gln
                                     45
gtt agg agt gct gac tgg tca ctt gaa gct tta ctc tac aaa tgg gat
                                                                      488
Val Arg Ser Ala Asp Trp Ser Leu Glu Ala Leu Leu Tyr Lys Trp Asp
                                 60
            55
atg aaa tgt gtc cac att cct ctt gag tct ttt gat gca gac aaa gaa
                                                                      536
Met Lys Cys Val His Ile Pro Leu Glu Ser Phe Asp Ala Asp Lys Glu .
                             75
gat ata gca gaa tot acc ott oca gga aga cat aca gtt gaa atg otg
Asp Ile Ala Glu Ser Thr Leu Pro Gly Arg His Thr Val Glu Met Leu
                         90
 gto att too tit goa aag gao agt oto tgaattatao otacaacotg
                                                                       631
 Val Ile Ser Phe Ala Lys Asp Ser Leu
```

100		105	a cotago			ccactt 691						
cagcttgaga	atgcagtgg	c tgatgagca g tctgaagat c tcatatgaa	g gtcaagt	ctg totgoo	ttag attt	gatgt 751						
aaaaaaaaa					,•=••	821						
<210> 73												
<211> 916 <212> DNA					•							
<213> Homo	sapiens											
<220>												
<221> CDS <222> 62	916 ·											
<221> sig_peptide												
<222> 62	757 Heijne mat:	riv				•						
scor	e 4.2											
seq	LVTPAALRPL	VLG/GN										
<221> poly <222> 904.												
	. 710											
<400> 73 cctgaatgac	ttgaatgtt	t ccccgcctg	a gctaaca	agtc catgtg	ggtg attc	agetet 60						
g atg gga	tgt gtt tt	c cag agc a	ca gaa ga	ac aaa cgt	ata ttc a	ag ata 109						
	-230		225		-220	-						
		cca gga gag Pro Gly Glu										
-215	* .	-210		-205	_	_						
		ctc agt gtg Leu Ser Val										
-200		-195		-190		-185						
		gac aac tta Asp Asn Leu										
caa gat gt	-180	gct gac cag	-17!		-17 or gaa arc							
Gln Asp Va	l Gln Glu	Ala Asp Gln	Gly Thr	Tyr Ile Cy	ys Glu Ile	Arg						
ctc aaa go	-165	cag gtg ttc	-160 aag aag	aca ata at	-155 ta ctg cat	gta 349						
Leu Lys Gl	y Glu Ser	Gln Val Phe	Lys Lys	Ala Val Va	al Leu His	Val						
	.50 .g gag ccc	-14 aaa gag ctc	_		140 gt gga ttg	att 397						
Leu Pro Gl	u Glu Pro	Lys Glu Leu -130	Met Val	His Val G	ly Gly Lev	Ile						
-135 cag atg gg	a tgt gtt	ttc cag agc	aca gaa		ac gtg acc	: aag 445						
Gln Met Gl	y Cys Val	Phe Gln Ser		Val Lys H								
-120 gta gaa tg		-115 tca gga cgg	cgc gca	-110 aag gag g	ag att gta							
Val Glu Tr	p Ile Phe	Ser Gly Arg	Arg Ala	Lys Glu G	lu Ile Val	Phe						
cgt tac ta	-100 c cac aaa	ctc agg atg	_		-							
Arg Tyr Ty	r His Lys -85	Leu Arg Met	Ser Ala	Glu Tyr S	er Gln Sen	Trp						
ggc cac tt	c cag aat	cgt gtg aac	ctg gtg	ggg gac a	tt ttc cg	aat 589						
Gly His Ph	e Gln Asn	Arg Val Asm	Leu Val	Gly Asp I	le Phe Arg	g Asn						
		ctt caa gga				a aac 637						

WO 99/31236 -53 - PCT/IB98/02122

Asp Gly Ser Ile Met Leu Gln Gly Val Arg Glu Ser Asp Gly Gly Asn -55 -50 -45												
tac acc tgc agt atc cac cta ggg aac ctg gtg ttc aag aaa acc att Tyr Thr Cys Ser Ile His Leu Gly Asn Leu Val Phe Lys Lys Thr Ile -40 -35 -30 -25	685											
gtg ctg cat gtc agc ccg gaa gag cct cga aca ctg gtg acc ccg gca Val Leu His Val Ser Pro Glu Glu Pro Arg Thr Leu Val Thr Pro Ala	733											
-20 -15 -10  gcc ctg agg cct ctg gtc ttg ggt ggt aat cag ttg gtg atc att gtg  Ala Leu Arg Pro Leu Val Leu Gly Gly Asn Gln Leu Val Ile Ile Val  -5 1 5	781											
gga att gtc tgt gcc aca atc ctg ctg ctc cct gtc ctg ata ttg atc Gly Ile Val Cys Ala Thr Ile Leu Leu Leu Pro Val Leu Ile Leu Ile 10 15 20	829											
gtg aag aag acc tgt gga aat aag agt tca gtg aat tct aca gtc ttg Val Lys Lys Thr Cys Gly Asn Lys Ser Ser Val Asn Ser Thr Val Leu	877											
gtg aag aac acg aag aat aac cca aaa aaa aaa aaa Val Lys Asn Thr Lys Lys Thr Asn Pro Lys Lys Lys Lys 45	916											
<210> 74 <211> 1153 <212> DNA <213> Homo sapiens												
<220> <221> CDS <222> 62520												
<221> polyA_signal <222> 11241129												
<221> polyA_site <222> 11411153												
<pre>&lt;400&gt; 74 cctgaatgac ttgaatgttt ccccgcctga gctaacagtc catgtgggtg attcagctct g atg gga tgt gtt ttc cag agc aca gta gac aaa tgt ata ttc aag ata Met Gly Cys Val Phe Gln Ser Thr Val Asp Lys Cys Ile Phe Lys Ile 1</pre>												
gac tgg act ctg tca cca gga gag cac gcc aag gac gaa tat gtg cta Asp Trp Thr Leu Ser Pro Gly Glu His Ala Lys Asp Glu Tyr Val Leu	157											
20 20												
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac cgc Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg	205											
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac cgc Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg 35 40 45 gta cac ttg atg ggg gac atc tta tgc aat gat ggc tct ctc ctg ctc Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu	205 253											
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac cgc Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg 35 40 45 gta cac ttg atg ggg gac atc tta tgc aat gat ggc tct ctc ctg ctc Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu Leu 50 55 60 caa gat gtg caa gag gct gac cag gga acc tat atc tgt gaa atc cgc Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg												
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac cgc Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg 35 40 45 gta cac ttg atg ggg gac atc tta tgc aat gat ggc tct ctc ctg ctc Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu Leu 50 55 60 caa gat gtg caa gag gct gac cag gga acc tat atc tgt gaa atc cgc Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg 65 70 75 80 ctc aaa ggg gag agc cag gtg ttc aag aag gcg gtg gta ctg cat gtg Leu Lys Gly Glu Ser Gln Val Phe Lys Lys Ala Val Val Leu His Val	253											
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac cgc Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg 40 45 gta cac ttg atg ggg gac atc tta tgc aat gat ggc tct ctc ctg ctc Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu Leu 50 55 60 caa gat gtg caa gag gct gac cag gga acc tat atc tgt gaa atc cgc Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg 65 70 75 80 ctc aaa ggg gag agc cag gtg ttc aag aag gcg gtg gta ctg cat gtg	253 301											

WO 99/31236 -54 - PCT/IB98/02122

Gln Met Gly Cys Val Phe Gln Ser Thr Glu Val Lys His Val Thr Lys	
115 120 125 gta gaa tgg ata ttt tca gga cgg cgc gca aag gta aca agg agg aaa	493
Val Glu Trp Ile Phe Ser Gly Arg Arg Ala Lys Val Thr Arg Arg Lys 130 135 140	173
cat cac tgt gtt aga gaa ggc tct ggc tgatggtatc aggacaaagg	540
His His Cys Val Arg Glu Gly Ser Gly 145 150	
tagaatcagg cacatgagga ggtgttgcaa gagcctgggc tttggtgctt atcagaactg	600
gacettetee tageaattte agetttetgg tgggaaaggt aacteeaatg aagaacaaga	660
acaagaagat gatgatgatg cttaactttt tggatgccga tatgagattg tacatgtaaa gcattttgta taagacttgg cccctgcatt ttagtttcct tctttctccc ttttccttcg	720 780
tatagagtoc atgggagaat gagggagatg atttttgtgg cocagocaag aaagcaatgg	840
gctagacatt aaaatgatta cacttttatt cttactgggg ttagttctgt gagttttcat	900
ctgtgcccca ttgccccatt tatgtgatgg agggaatttt catgggtact tcacgtgttg	960
ggattgattg atcctggggg ccagggtgaa gggtatttta cgggacctct ataaagcagg	1020
aagaagcaag tthattottt agaccagtag ototoaacca tgatgtggto atatatttat gggtoaacat gtgttgtggg gatatoocaa gtaacttgtt attaataaaa gttaagttgo	1080 1140
aaaaaaaaaa aaa	1153
<210> 75 <211> 1517	
<212> DNA -	
<213> Homo sapiens	
<220>	
<221> CDS <222> 21167	
(222) 21107	
<400> 75	
ctctgaaatg cttgtctttt afg ctg gna ggt gac cat agg gct ctg ctt tta Met Leu Xaa Gly Asp His Arg Ala Leu Leu	53
Met Leu Xaa Gly Asp His Arg Ala Leu Leu 1 5 10	101
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 5 10 aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca	
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25	101
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct	
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro	101
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40	101
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro	101
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45	101 149 197
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt	101 149 197 257
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt	101 149 197
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat	101 149 197 257 317
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta	101 149 197 257 317 377 437 497
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagttagg tctttaaagga aagcaacgct cctctgaaat gcttgtcttt tatgctggga ggtgaccata gggctctgct ::taaaagata tggctgcttc	101 149 197 257 317 377 437 497 557
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagtcagg tctttaaagga aagcaacgct cctctgaaat gcttgtcttt tatgctggga ggtgaccata gggctctgct ttaaaagata tggctgctc aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagag	101 149 197 257 317 377 437 497 557 617
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagttagg tctttaaagga aagcaacgct cctctgaaat gcttgtcttt tatgctggga ggtgaccata gggctctgct ttaaaagata tggctgcttc aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagag	101 149 197 257 317 377 437 497 557 617 677
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagtcagg tctttaagga aagcaacgct cctctgaaat gcttgtcttt tatgctggga ggtgaccata gggctctgct tttaaagata tggctgctc aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagag	101 149 197 257 317 377 437 497 557 617
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcttaac cattcaccaa gagccaatat ctttgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtcttt tatgctgga ggtgaccata gggctctgct tttaaagata tggctgtct aaaggccaga gtcacaggaa ggtgaccata gggctctgct tttaaagata tggctgttc aaaggccaga gtcacaggaa ggtgaccata gggctctgct tttaaagata tggctgtctc aaaggccaga gtcacaggaa ggacttcttc caggagatt aattgtcac cttctaatgc aagggtctca cactgtgaac cacttaggat gtgatcactt tcaggtggc aggaggagag ttaaaaatgac ctcatgtcat tcttgtccac ggttttgttg agttttcact cttctaatgc aagggtctca cactgtgaac cacttaggat gtgatcactt tcaggtggc aggaatgttg aaggttttt cactaggtt ggtatcactt tcaggtggc aggaatgttg aaggttttt ggctctttt ggtatttt tttaaaaaaag atatctattt gaaagttctc aggattgtac	101 149 197 257 317 377 437 497 557 617 677 737
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1	101 149 197 257 317 377 437 497 557 617 677 737 797 857 917
Mét Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 10 aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25 ggg aga tta gtg gtg atg gag agg agg gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40 tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45 cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta ttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtcttt tatgctgga ggtgaccata gggctctgct tattaaaatgc gatctgtct tcttgtcac ggttgtgt agattgttc caagggccaatat tcttgtctt tatgctgga ggtgaccata gggctctgct tataaaatga ctcattgtcc tcttgtcac ggttttgttg aggttagg ctcataggat ggtgaccat agtgtgtgt aggttgtgt agattgttc aaaggccaga ctcatggaa ggctctcc cagggagatt tcagggtgcc aggaaggagag ttaaaaatgac ctcatgtca tcttgtcaca ggtttttgttg agttttcact ctctaatgc aaaggtcttc cactggaac cacttaggat gtgaccact tcagggtgcc aggaaggagag ctatgtttt aaaggatctc aaaggtctca tcttgtaaaaaaa atatctatt gaaagttctc aaggatgtaa aatatttt gaaagttct aaaggttctc aaggatgtta cacttaggat gtgaccact tctcaaacca ttcaacaagg acaatatct aaggattttc ttggtagcac aaattttct tattgcttaa aaagttct tcctaaacca ttcaacaaga gcaaatatct aaggattttc ttggtagcac aaattttct aatgcttaga aaattgcct ccttgttatt tctgtttgta agacttaagt gagttaggt ctttaatt tattgcttaa aaagtttct tcctaaacca ttcaacaaga gcaaatatct aaggattttc ttggtagcac aaattttctt aatgcttaga aaattgcct ccttgttatt tctgtttgta agacttaagt gagttaaggt ctttaattt tattgcttaga aaattgcct ccttgttatt tctgtttgta agacttaagt gagttaggt ctttaaggaa gcaaatttt tcttgttaga aaattgcct ccttgttatt tcttgttatt tctgtttgta agacttaagt gagttaggt ctttaaggaa gcaaacgct ccttgtaacaaga gcaaatttct tctgttaga aaattgcct ccttgttatt tctgtttatt tctgtttgta aaattgcct ccttgttatt tctgtttatt tctgtttgta aaattgcct ccttgtaacaaga gcaaacgct c	101 149 197 257 317 377 437 497 557 617 677 737 797 857 917
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg agg gat aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt cattaaaaa agatatctat ttcagagtgt cattacacag gatctgaca taaaagttc ttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta ttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtctt tatgctgga ggtgaccata gggctctgct ttaaaagata tggctgctc aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagg ttaaaatgac ctcatgtcct tcttgtccac ggttttgttg agttttcact cacttagga gccaatatct cacttaggat gtgatcactt tcaggtggc aggaggagg ttaaaatgac ctcatgtcac tcttgaaaaa aaattttc taaagtgccaatagtctc aagggtctca cactgtgaac cacttaggat gtgatcactt tcaggtggc aggatggtca aatgtcttt gccagttca tttaaaaaaa ataactactt taaagttcc aatgtttca cagtacagga tctgaacaa aaagttctt tccaaacca ttcaaccaaga gccaatatct aggcatttc tctggtagcac aaatttctt taaaggaaa agacttcc tttgttatt tctgtttgta agacttaagt gagttaggtc ttaaagaaa aaattgtcc tcttgttatt tctgttttaa agacttaagt gagttaggtc ttaaagaaa aaattgtcc tcttgttatt tctgttttta agacttaagt gagttaggtc ttaaagaaa aaattgtcc tcttgttatt tctgttttaa agacttaagt gagttaggtc ttaaagaaa aaattgtcc tcttgttatt tctgttttta agacttaagt gagttaggtc ttaaagaaa aaattgcct tctgaaatgc ttgtctttna tgctgggagg tgaccataagg	101 149 197 257 317 377 437 497 557 617 677 737 797 857 917 977
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg agg ggt t aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt cattaaaaa agatatctat tgaaagttc tcagagattgt acatatgttt cacagtacag gatctgaca taaaagttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtcttt tatgctgga ggtgaccata gggctctgct ttaaagata tggctgctc aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagg ttaaaatgac ctcatgtcet tcttgtccac gggttttgttg agttttcact cttcttaatgc aagggtctca cactgtgaac cacttaggat gtgatcactt tcaggtggc aggaatgttg aatgtctttg gctcagttca tttaaaaaag atatctatt gaaagttctc agagattgta atatgtttca cagtacagga tctgtacata aaagttctt tcaggtggc aggattgtca atatgtttca cagtacagga tctgtacata aaagttctt tctgataga aaattttct ccttgttatt tctgtttgta agacttaagt gagttaggtc tttaagaa aaatttgct ccttgttatt tctgtttgta agacttaagt gagttaggtc tttaagaaa gccaatatct tctgtttgta agacttaagt gagttaggtc tttaagaaa gccaatatct tctgtttgta agacttaagt gagttaggtc tttaagaaa gctactctttaaagaa gccaatatc tctgtacaata gagctaatagg tctgaaatgc ttgtctttna tgctgggagg tgaccataagg gctgctcaa aggacttca aggacttcaa aggctccttaaagagtctcaa aggacttcaa aggctcctttaaagaatatcg	101 149 197 257 317 377 437 497 557 617 677 737 797 857 917 977 1037
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 10 10 aag ata tgg ctg ctt caa agg cca gga tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25 ggg aga tta gtg gtg atg gag agg agg gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40 tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45 cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtct tggctcagtt catttaaaaa agatatcat ttgaaagttc tcagagttgt accatatgtt tcaggcatt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctcttgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gtctgcttt tatgctggaa ggaccataa gggctctcc cagggagtt tttaaaaatgac ctcatgtgac cacttaggat gtgaccata gggtttttttt tattgctta gattttcact ttaaaggacag gtcacaggaa ggacttctc cagggagatt tttcaagga ggagtctct tcttgtcac gatttttttaatgtta gattttcact taaggccaga gtcacaggaa ggacttctc cagggagatt agtggtgatg gagaggaggaggtca accattaggat gtctttaattt gattttaact aaggctctca aagggtcca cacttaggat gtctttattt gattttcact tcttgtcac cacttaggat gtctttatt tcaggtgac cacttaggat gtgatcact tcaggtggc aagaatgttg aaggattttc tcttgtcac ggtttttttt tattgctta aaggtttca tcttgacac aacttaggat gtgatcact tcaggtggc aaggatgtgaa gacaatatct aggcatttc tcttgtcac ggtttttttt tattgctta aaggttgtac atttgacat aaggttctc tcttgtcac ggtttttttt tattgctta aaggttgtac aatttttt tcttgttta tcttgttgaa gacatatct tcttgtcac ggtttttttt tccacaaga gccaatatct aggcattttc tctgtacata aaagtttctt tctaaacaa aaattttct tattgcttaaa aaattgtcc ccttgtaaatt tcttgtttgaa gacattaagt gaccataagg gccaatatct tcttgttaa agacttaagt gaccataagg gccaatatct tcttgtttaa agacttaagt gaccataagg gaccataagg ccaaggatg tctttaaagaa agcaacgctcc tcttgtaaatg ttgtctttna tgctggagg gaccataagg gaccataagg tctttcaca ggagattatg tcttaaagaaatg tctttaaagaaa gccaacgctcc tcttgaaatg taaaatgacct cattgtctt ttaaaaaagg ccaaggatg gaccataagg tcttttaaaga agcaccatagg taaaatgacct taaaagaaga gaccacatagg ttggatgaagat aaaatgacct taaaagaaga cacaaggagg acttcttca ggagaagat taaaatgacct taaaatgacct tctttaaaga	101 149 197 257 317 377 437 497 557 617 677 737 797 857 917 977 1037 1097
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg agg ggt t aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt cattaaaaa agatatctat tgaaagttc tcagagattgt acatatgttt cacagtacag gatctgaca taaaagttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtcttt tatgctgga ggtgaccata gggctctgct ttaaagata tggctgctc aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagg ttaaaatgac ctcatgtcet tcttgtccac gggttttgttg agttttcact cttcttaatgc aagggtctca cactgtgaac cacttaggat gtgatcactt tcaggtggc aggaatgttg aatgtctttg gctcagttca tttaaaaaag atatctatt gaaagttctc agagattgta atatgtttca cagtacagga tctgtacata aaagttctt tcaggtggc aggattgtca atatgtttca cagtacagga tctgtacata aaagttctt tctgataga aaattttct ccttgttatt tctgtttgta agacttaagt gagttaggtc tttaagaa aaatttgct ccttgttatt tctgtttgta agacttaagt gagttaggtc tttaagaaa gccaatatct tctgtttgta agacttaagt gagttaggtc tttaagaaa gccaatatct tctgtttgta agacttaagt gagttaggtc tttaagaaa gctactctttaaagaa gccaatatc tctgtacaata gagctaatagg tctgaaatgc ttgtctttna tgctgggagg tgaccataagg gctgctcaa aggacttca aggacttcaa aggctccttaaagagtctcaa aggacttcaa aggctcctttaaagaatatcg	101 149 197 257 317 377 437 497 557 617 677 737 797 857 917 977 1037

1457

agttgtacat atgtttcaca gtacaggate tgtacataaa agtttettte etaaaccatt caccaagage caatatetag geattteett ggtageacaa attttettat tgettagaaa

attgtcctcc ttgttatttc tgtttgtaag acttaagtga gttaggtctt taaggaaagc aacgeteete tgaaatgett gtettttatg etgggaggtg accataggge tetgetttta <210> 76 <211> 526 <212> DNA... <213> Homo sapiens <220> <221> CDS <222> 22***318 <221> sig_peptide <222> 22..93 <223> Von Heijne matrix score 4.6 seq FFIFCSLNTLLLG/GV <221> polyA_signal <222> 497..502 <221> polyA_site <222> 516..526 51 ctgcctgctg cttgctgcac c atg aag tct gcc aag ctg gga ttt ctt cta Met Lys Ser Ala Lys Leu Gly Phe Leu Leu -20 99 aga tto tto ato tto tgo toa ttg aat acc ctg tta ttg ggt ggt gtt Arg Phe Phe Ile Phe Cys Ser Leu Asn Thr Leu Leu Gly Gly Val -5 -10 aat aaa att gcg gag aag ata tgt gga gac ctc aaa gat ccc tgc aaa 147 Asn Lys Ile Ala Glu Lys Ile Cys Gly Asp Leu Lys Asp Pro Cys Lys 10 ttg gac atg aat ttt gga agc tgc tat gaa gtt cac ttt aga tat ttc 195 Leu Asp Met Asn Phe Gly Ser Cys Tyr Glu Val His Phe Arg Tyr Phe 25 30 tac aac aga acc tee aaa aga tgt gaa act ttt gte tte tee gge tgt 243 Tyr Asn Arg Thr Ser Lys Arg Cys Glu Thr Phe Val Phe Ser Gly Cys 50 45 40 aat ggc aac ctt aac aac ttc aag ctt aaa ata gaa cgt gaa gta gcc 291 Asn Gly Asn Leu Asn Asn Phe Lys Leu Lys Ile Glu Arg Glu Val Ala 60 55 338 tgt gtt gca aaa tac aaa cca ccg agg tgagaggatg tgaactcatg Cys Val Ala Lys Tyr Lys Pro Pro Arg aagttgtctg ctgcaccatc cgaaataaag acacaagaaa attcagactg attttgaaat 398 ctttgtaata tttccataat gctttaagct tccatatgtt tgctattttc ctgaccctag 458 ttttgtcttt cctggaaatt aactgtatga tcattagaat gaaagagtct ttctgtcaaa 518 526 aaaaaaaa

<210> 77 <211> 352 <212> DNA <213> Homo sapiens

```
<220>
<221> CDS
<222> 8..292
<221> sig peptide
<222> 8..118
<223> Von Heijne matrix
     score 5.6
     seg WLLLDALLRLGDT/KK
<221> polyA_signal
<222> 317..322
<221> polyA site
<222> 339..352
<400> 77
ctgagat atg gca agt ccc gct gta aac agg tgg aaa agg cca agg ttg
                                                                      49
        Met Ala Ser Pro Ala Val Asn Arg Trp Lys Arg Pro Arg Leu
                                    -30
aag ccg gtg tgg cca cgg cgc ttg gaa tcc tgg ttg ttg ctg gat gct
Lys Pro Val Trp Pro Arg Arg Leu Glu Ser Trp Leu Leu Leu Asp Ala
            -20
                                -15
ctt ttg cga tta gga gat acc aaa aaa aag cga cag cct gaa gca gcc
                                                                     145
Leu Leu Arg Leu Gly Asp Thr Lys Lys Lys Arg Gln Pro Glu Ala Ala
       - 5
                           1
aca aaa too tgt gtt aga ago ago tgt ggg ggt ooc agt gga gat ggg
                                                                     193
Thr Lys Ser Cys Val Arg Ser Ser Cys Gly Gly Pro Ser Gly Asp Gly
                                                            25
                                        20
                   15
cct ccc cca tgc ctc cag cag cct gac cct cgt gcc ctg tct cag gcg
                                                                     241
Pro Pro Pro Cys Leu Gln Gln Pro Asp Pro Arg Ala Leu Ser Gln Ala
                                    35
               30
                                                                     289
tto tot aga too ttt cot otg ttt coc tot ctc get ggc aaa agt atg
Phe Ser Arg Ser Phe Pro Leu Phe Pro Ser Leu Ala Gly Lys Ser Met
                             5 Ó
                                                    55
            45
                                                                      342
atc taattgaaac aagactgaag gatcaataaa cagccatctg ccccttcaaa
Ile
                                                                      352
aaaaaaaaa
```

<211> 542

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 16..378

<221> sig_peptide

<222> 16..84

<223> Von Heijne matrix
 score 9.8
 seq FLLFFFLFLLTRG/SL

<221> polyA_signal

<222> 502..507

<221> polyA_site

<222> 522..542

<400> 78	
cacgacctgt gggcc atg atg cta ccc caa tgg ctg ctg ctg ctg ttc ctt  Met Met Leu Pro Gln Trp Leu Leu Leu Phe Leu	51
-20 -15 ctc ttc ttc ttc ctc ctc ctc acc agg ggc tca ctt tct cca aca Leu Phe Phe Leu Phe Leu Leu Thr Arg Gly Ser Leu Ser Pro Thr -10 -5 1 5	99
aaa tat aac ctt ttg gag ctc aag gag tct tgc atc cgg aac cag gac Lys Tyr Asn Leu Leu Glu Leu Lys Glu Ser Cys Ile Arg Asn Gln Asp 10 15 20	147
tgc gag act ggc tgc tgc caa cgt gct cca gac aat tgc gag tcg cac Cys Glu Thr Gly Cys Cys Gln Arg Ala Pro Asp Asn Cys Glu Ser His 25 30 35	195
tgc gcg gag aag ggg tcc gag ggc agt ctg tgt caa acg cag gtg ttc Cys Ala Glu Lys Gly Ser Glu Gly Ser Leu Cys Gln Thr Gln Val Phe 40 45	243
ttt ggc caa tat aga gcg tgt ccc tgc ctg cgg aac ctg act tgt ata Phe Gly Gln Tyr Arg Ala Cys Pro Cys Leu Arg Asn Leu Thr Cys Ile 55 60 65	291
tat toa aag aat gag aaa tgg ott ago ato goo tat ggo ogt tgt cag Tyr Ser Lys Asn Glu Lys Trp Leu Ser Ile Ala Tyr Gly Arg Cys Gln 70 85	339
aaa att gga agg cag aag ttg gct aag aaa atg ttc ttc tagtgctccc Lys Ile Gly Arg Gln Lys Leu Ala Lys Lys Met Phe Phe 90 95	388
teettettge tgeeteetee teeteeaeet geteteetee etaeeeagag etetgtgtte accetgttee ceagageete caccatgagt ggagggaagt ggggagtgat tgaaataaag agetttttea atgaaaaaaa aaaaaaaaaa	448 508 542
<210> 79 <211> 233 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 57233	
<400> 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg Met . 1	59
atc cta tgt ttc ctt ctt cct cat cat cgt ctt cag gaa gcc aga cag  Ile Leu Cys Phe Leu Leu Pro His His Arg Leu Gln Glu Ala Arg Gln  5 10 15	107
att caa gta ttg aag atg ctg cca agg gaa aaa tta aga aga aga gaa Ile Gln Val Leu Lys Met Leu Pro Arg Glu Lys Leu Arg Arg Glu 20 25 30	155
gag aga aaa caa ata aat ggg aaa aaa gaa agg aca aaa tat gaa aca Glu Arg Lys Gln Ile Asn Gly Lys Lys Glu Arg Thr Lys Tyr Glu Thr 35 40 45	203
cca aga aaa aga gaa gga aaa aaa aaa aaa Pro Arg Lys Arg Glu Gly Lys Lys Lys 50 55	233

<210> 80 <211> 660 <212> DNA WO 99/31236 -58- PCT/IB98/02122

```
<213> Homo sapiens
<220>
<221> CDS
<222> 83..340
<221> sig_peptide
<222> 83..124
<223> Von Heijne matrix
      score 7.5
      seq VALNLILVPCCAA/WC
<221> polyA_signal
<222> 573..578
<221> polyA site
<222> 607..660
<400> 80
gaatttgtaa aacttctgct cgtttacact gcacattgaa tacaggtaac taattggaag
                                                                      60
gagaggggag atcactcttt tg atg gtg gcc ctg aac ctc att ctg gtt ccc
                                                                     112
                         Met Val Ala Leu Asn Leu Ile Leu Val Pro
                                         -10
tgc tgc gct gct tgg tgt gac cca cgg agg atc cac tcc cag gat gac
                                                                     160
Cys Cys Ala Ala Trp Cys Asp Pro Arg Ile His Ser Gln Asp Asp
                                5
gtg ccc cgt age tet get get gat act ggg tet geg atg cag egg egt
                                                                     208
Val Pro Arg Ser Ser Ala Ala Asp Thr Gly Ser Ala Met Gln Arg Arg
                            20
       15
gag gcc tgg gct ggt tgg aga agg tca caa ccc ttc tct gtt ggt ctg
                                                                      256
Glu Ala Trp Ala Gly Trp Arg Arg Ser Gln Pro Phe Ser Val Gly Leu
                        35
                                                                      304
cet tet get gaa aga ete gag aac caa eea ggg aag etg tee tgg agg
Pro Ser Ala Glu Arg Leu Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg
45
                    50
                                        55
tee etg gte gga gag gga tat aga ate tgt gae ete tgacaaetgt
                                                                      350
Ser Leu Val Gly Glu Gly Tyr Arg Ile Cys Asp Leu
                                    70
                                                                      410
gaagccaccc tgggctacag aaaccacagt cttcccagca attattacaa ttcttgaatt
ccttggggat tttttactgc cctttcaaag cacttaagtg ttagatctaa cgtgttccag
                                                                      470
tgtctgtctg aggtgactta aaaaatcaga acaaaacttc tattatccag agtcatggga
                                                                      530
                                                                      590
gagtacaccc tttccaggaa taatgttttg ggaaacactg aaatgaaatc ttcccagtat
tataaattgt gtatttaaaa aaagaaactt ttctgaatgc ctacctggcg gtgtatacca
                                                                      650
                                                                      660
ggcagtgtgc
<210> 81
<211> 605
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
```

<222> 47..541

<221> sig_peptide <222> 47..220

<223> Von Heijne matrix score 5.4

seq QLLDSVLWLGALG/LT

<221> polyA_site <222> 597..605 <400> 81 55 aaagtgggag gagcactagg tetteeegte acetecacet etetee atg ace egg Met Thr Arg ctc tgc tta ccc aga ccc gaa gca cgt gag gat ccg atc cca gtt cct 103 Leu Cys Leu Pro Arg Pro Glu Ala Arg Glu Asp Pro Ile Pro Val Pro -55 -50 -45 151 cca agg ggc ctg ggt gct ggg gag ggg tca ggt agt cca gtg cgt cca Pro Arg Gly Leu Gly Ala Gly Glu Gly Ser Gly Ser Pro Val Arg Pro - 35 -30 cct gta tcc acc tgg ggc cct agc tgg gcc cag ctc ctg gac agt gtc 199 Pro Val Ser Thr Trp Gly Pro Ser Trp Ala Gln Leu Leu Asp Ser Val -20 -15 -10 247 cta tgg ctg ggg gca cta gga ctg aca atc cag gca gtc ttt tcc acc Leu Trp Leu Gly Ala Leu Gly Leu Thr Ile Gln Ala Val Phe Ser Thr 1 act ggc cca gcc ctg ctg ctt ctg gtc agc ttc ctc acc ttt gac 295 Thr Gly Pro Ala Leu Leu Leu Leu Leu Val Ser Phe Leu Thr Phe Asp 15 20 ctg ctc cat agg ccc gca ggt cac act ctg cca cag cgc aaa ctt ctc Leu Leu His Arg Pro Ala Gly His Thr Leu Pro Gln Arg Lys Leu Leu 30 35 391 acc agg ggc cag agt cag ggg gcc ggt gaa ggt cct gga cag cag gag Thr Arg Gly Gln Ser Gln Gly Ala Gly Glu Gly Pro Gly Gln Gln Glu 50 45 439 get eta ete etg caa atg ggt aca gte tea gga caa ett age ete cag Ala Leu Leu Gln Met Gly Thr Val Ser Gly Gln Leu Ser Leu Gln 65 487 gac gca ctg ctg ctg ctc atg ggg ctg ggc ccg ctc ctg aga gcc Asp Ala Leu Leu Leu Leu Met Gly Leu Gly Pro Leu Leu Arg Ala 75 80 tgt ggc atg ccc ttg acc ctg ctt ggc ctg gct ttc tgc ctc cat cct 535 Cys Gly Met Pro Leu Thr Leu Leu Gly Leu Ala Phe Cys Leu His Pro 100 95 591 tgg gcc tgagagcccc tccccacaac tcagtgtcct tcaaatatac aatgaccacc 605 cttcttcaaa aaaa

<210> 82

<211> 396

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 46..285

<221> sig_peptide

<222> 46..150

<223> Von Heijne matrix score 3.6 seq LEPGLSSSAACNG/KE

<221> polyA_signal

<222> 364..369

<221> polyA_site

<222> 385..396

WO 99/31236 -60- PCT/IB98/02122

<400> 82

cctctacagg aatcagactc agcctctttt ggttttcagt gaagt atg cct ttt caa Met Pro Phe Gln -35	57										
ttt gga acc cag cca agg agg ttt cca gtg gaa gga gat tct tca Phe Gly Thr Gln Pro Arg Arg Phe Pro Val Glu Gly Gly Asp Ser Ser -30 -25 -20	105										
att gag ctg gaa cct ggg ctg agc tcc agt gct gcc tgt aat ggg aag Ile Glu Leu Glu Pro Gly Leu Ser Ser Ala Ala Cys Asn Gly Lys -15 -10 -5 1	153										
gag atg toa oca acc agg caa oto ogg agg tgo oot gga agt cat tgo Glu Met Ser Pro Thr Arg Gln Leu Arg Arg Cys Pro Gly Ser His Cys 5 10 15	201										
ctg aca ata act gat gtt ccc gtc act gtt tat gca aca acg aga aag Leu Thr Ile Thr Asp Val Pro Val Thr Val Tyr Ala Thr Thr Arg Lys 20 25 30	249										
cca cct gca caa agc agc aag gaa atg cat cct aaa tagcaccatt Pro Pro Ala Gln Ser Ser Lys Glu Met His Pro Lys 35 40 45	295										
aagtotttig toaaggtotg actaggtoaa gggtaatgga coagtatoat otggtgatot ggtaaacaaa taaaagtggt ggcacottoa aaaaaaaaaa a	355 396										
<210> 83											
<211> 432 <212> DNA	•										
<213> Homo sapiens											
<220> <221> CDS <222> 22240											
<221> sig_peptide <222> 2284											
<222> 2284  <223> Von Heijne matrix score 12 seq VLVLCVLLLQAQG/GY											
<221> polyA_signal <222> 397402											
<221> polyA_site <222> 421432											
<400> 83 getcaegete tggteagagt t atg gea eee eag act etg etg eet gte etg	51										
Met Ala Pro Gln Thr Leu Leu Pro Val Leu -20 -15											
gtt ctc tgt gtg ctg ctg ctg cag gcc cag gga gga tac cgt gac aag Val Leu Cys Val Leu Leu Gln Ala Gln Gly Gly Tyr Arg Asp Lys -10 -5 1 5	99										
atg agg atg cag aga atc aag gtc tgt gag aag cga ccc agc ata gat Met Arg Met Gln Arg Ile Lys Val Cys Glu Lys Arg Pro Ser Ile Asp 10 15 20	147										
cta tgc atc cac cac tgt tca tgt ttc caa aag tgt gaa aca aat aag Leu Cys Ile His His Cys Ser Cys Phe Gln Lys Cys Glu Thr Asn Lys 25 30 35	195										
ata tgc tgt tca gcc ttc tgt ggg aac att tgt atg agc atc cta Ile Cys Cys Ser Ala Phe Cys Gly Asn Ile Cys Met Ser Ile Leu 40 45 50	240										

tga tgc	gtgg	gag	cgaa	ggct gcac	99 9 aa g	atgt gaca	gcat tcaa	c ct a tc	gctc atca	cctg gcac	aac	cctt aaca	cca tca	teega acago	agactg gaatgc	300 360
cac	cctc	ccc	agtg	tctg	aa c	tccc	tgtc	c ct	gtca	aatg	aac	caga	aca	aatq	ccatg	420
	aaaa											_		-	_	432
ť																
<21	0> 8	4														•
<21	1> 4	20														
	2 > D															
<21	3 > H	omo	sapi	ens												
. 22	٥.															
<22	0> 1> C	De														
	2 > B		82													
		<b>.</b>	~-													
<22	1> p	olyA	_site	е												
<22	2 > 4	08	420													
	_															
	0 > 8															
gee	race	cga ·	CCCC	catg	c g	CCTCI	tgtag	ggt	agaaq	gaag	tate	gtct	tcc	tggad	cccct	60
990	بعود	get .	gtaad	Jaaag	ja C	ccati								gag g Glu (		112
								ייבני ו	ueu (	JIY A	11a C		1111	Jiu (	stu.	
aag	ctg	ttt	gat	gcc	ccc	ttg	tcc	atc	agc	aag	-	-	caq	ctq	gaa	160
Lys	Leu	Phe	Asp	Ala	Pro	Leu	Ser	Ile	Ser	Lys	Arg	Glu	Gln	Leu	Glu	
	10					15					20					
cag	cag	gtc	cca	gag	aac	tac	ttc	tat	gtg	cca	gac	ctg	ggc	cag	gtg	208
GIN 25	GIn	Val	Pro	Glu		Tyr	Phe	Tyr	Val		Asp	Leu	Gly	Gln		
	G2G	a++	~a+	a++	30	* * * *				35					40	25.6
Pro	Glu	Tle	gat Asp	Val	Pro	Ser	Tur	Len	Dro	gac Acn	Lau	Dro.	ggc	Tlo	gcc	256
				45			• 7 =	DCu	50	nop	Deu	110	Gly	55	A14	
aac	gac	ctc	atg	tac	att	gcc	gac	ctg		ccc	ggc	att	qcc		tct	304
Asn	Asp	Leu	Met	Tyr	Ile	Ala	Asp	Leu	Gly	Pro	Gly	Ile	Āla	Pro	Ser	
			60					65	-				70			
			acc													352
Ala	Pro		Thr	Ile	Pro	Glu		Pro	Thr	Phe	His		Glu	Val	Ala	
a a a	cct	75 65.6	336	366	+	226	80					85				400
Glu	Pro	Len	aag Lys	Thr	TVr	Lve	Mer	999	Tur	Laac	agea	ice a	acca	cege	:0	402
	90		-,-	****	- / -	95		O.,	- 7 -							
ccac	caaa	aa a	aaaa	aaa												420
	_	_	•													
	)> 85								_							
	L> 5(	_							•							
< 4 1 4	?> Dî	4A														

<213> Homo sapiens

<220>

<221> CDS

<222> 80..415

<221> sig_peptide <222> 80. 142 <223> Von Heijne matrix score 5.4 seq TFCLIFGLGAVWG/LG

<221> polyA_signal

WO 99/31236 -62- PCT/IB98/02122

<222> 471476	
<221> polyA_site	
<222> 488501	
<400> 85	
cocgettgat tecaagaace tettegatat ttattttat ttttaaagag ggagacgatg	60
gactgagetg atcegeace atg gag tet egg gte tta etg aga aca tte tgt  Met Glu Ser Arg Val Leu Leu Arg Thr Phe Cys  -20  -15	112
ttg atc ttc ggt ctc gga gca gtt tgg ggg ctt ggt gtg gac cct tcc	160
Leu Ile Phe Gly Leu Gly Ala Val Trp Gly Leu Gly Val Asp Pro Ser -10 -5 1 5	
cta cag att gac gtc tta aca gag tta gaa ctt ggg gag tcc acg acc Leu Gln Ile Asp Val Leu Thr Glu Leu Glu Leu Gly Glu Ser Thr Thr	208
10 15 20	
gga gtg cgt cag gtc ccg ggg ctg cat aat ggg acg aaa gcc ttt ctc	256
Gly Val Arg Gln Val Pro Gly Leu His Asn Gly Thr Lys Ala Phe Leu 25 30 35	
ttt caa gat act ccc aga agc ata aaa gca tcc act gct aca gct gaa	304
Phe Gln Asp Thr Pro Arg Ser Ile Lys Ala Ser Thr Ala Thr Ala Glu 40 45 50	
cag ttt ttt cag aag ctg aga aat aaa cat gaa ttt act att ttg gtg	352
Gln Phe Phe Gln Lys Leu Arg Asn Lys His Glu Phe Thr Ile Leu Val 55 60 65 70	
acc cta aaa cag acc cac tta aat tca gga gtt att ctc tca att cac	400
Thr Leu Lys Gln Thr His Leu Asn Ser Gly Val Ile Leu Ser Ile His	
75 80 85 cac ttg gat cac agg taaatgtggt tgctggagtt tcctgtgttt tcattatatg	455
His Leu Asp His Arg	
90 tggttaaatg aatatattaa agagaagtaa acaaaaaaaa aaaaaa	501
eggerated ancadatora adadatata acatatata acatata	
<210> 86	
<211> 454	
<212> DNA <213> Homo sapiens	
•	
<220> <221> CDS	
<222> 152361	
<221> sig_peptide <222> 152283	
<223> Von Heijne matrix	
score 4.7 seq:FLLSLSLITYCFW/DP	
Seq. I be be be the sequence of the sequence o	
<400> 86	
	60
gacattttac ttttttctgt taacgcttac cctagaaatt agaaatgaca ccacgtattc ttagcgaagt ccagttttca gcattttgtc cttattggac aatagcaagg atattagaac	60 120
ttagcgaagt ccagttttca gcattttgtc cttattggac aatagcaagg atattagaac gtgttggttc cgcgtgcttc cgtcttgagt t atg tgc tgc tat tgt cgg ata	
ttagcgaagt ccagttttca gcattttgtc cttattggac aatagcaagg atattagaac gtgttggttc cgcgtgcttc cgtcttgagt t atg tgc tgc tat tgt cgg ata Met Cys Cys Tyr Cys Arg Ile	120
ttagcgaagt ccagttttca gcattttgtc cttattggac aatagcaagg atattagaac gtgttggttc cgcgtgcttc cgtcttgagt t atg tgc tgc tat tgt cgg ata	120
ttagcgaagt ccagttttca gcattttgtc cttattggac aatagcaagg atattagaac gtgttggttc cgcgtgcttc cgtcttgagt t atg tgc tgc tat tgt cgg ata  Met Cys Cys Tyr Cys Arg Ile  -40  ttt tgt ctt aga tgt acg tac ttt cct gtt cat tgt ggt atg tgt aat Phe Cys Leu Arg Cys Thr Tyr Phe Pro Val His Cys Gly Met Cys Asn	120 172
ttagcgaagt ccagttttca gcattttgtc cttattggac aatagcaagg atattagaac gtgttggttc cgcgtgcttc cgtcttgagt t atg tgc tgc tat tgt cgg ata Met Cys Cys Tyr Cys Arg Ile -40  ttt tgt ctt aga tgt acg tac ttt cct gtt cat tgt ggt atg tgt aat Phe Cys Leu Arg Cys Thr Tyr Phe Pro Val His Cys Gly Met Cys Asn -35 -30 -25	120 172
ttagcgaagt ccagttttca gcattttgtc cttattggac aatagcaagg atattagaac gtgttggttc cgcgtgcttc cgtcttgagt t atg tgc tgc tat tgt cgg ata  Met Cys Cys Tyr Cys Arg Ile  -40  ttt tgt ctt aga tgt acg tac ttt cct gtt cat tgt ggt atg tgt aat Phe Cys Leu Arg Cys Thr Tyr Phe Pro Val His Cys Gly Met Cys Asn	120 172 220

WO 99/31236 -63- PCT/IB98/02122

act tac tgc ttt tgg gac cec cec cat egg ggt tca cat tec etc tec	316
Thr Tyr Cys Phe Trp Asp Pro Pro His Arg Gly Ser His Ser Leu Ser	
-5 1 5 10	,
cta gag cac act ccc ttg gat ttc ctc gag tgg ggt ctg ctg cgg	361
Leu Glu His Thr Pro Leu Asp Phe Leu Glu Trp Gly Leu Leu Arg	
15 20 25	
tgaagctttc ccattttatg tgcagattat tttcagaggg tatatagaat tcaggcag	
gtttcgttgt agcacattaa aaatattttc ccc	454
<210> 87	
<211> 1272	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 32307	
<221> sig_peptide	
<222> 3270	
<223> Von Heijne matrix	
score 4.2	
seq MLFSLSLLSNLNQ/IG	
004	
<221> polyA_signal	
<222> 12401245	
2001. malub miba	
<221> polyA_site	
<222> 12611272	
<400× 87	
<pre>&lt;400&gt; 87 gtcaggttgc accecettt ggttcccgag c atg ctg ttt tct ctc agc ctt</pre>	52
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt	
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt Met Leu Phe Ser Leu Ser Leu -10	
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca	.c 100
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt Met Leu Phe Ser Leu Ser Leu -10	c 100
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi	c 100 s
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5  1 5 10	c 100 s
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5  1  5  10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca	c 100 s
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca  Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca  Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl	100 s a 148
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca  Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca  Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25	100 s a 148 n
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca  Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca  Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca	100 s a 148 n
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca  Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca  Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca  Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa	100 s a 148 a 148 a 196 a 244
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca  Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca  Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca  Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40	100 s a 148 a 148 a 196 a 244
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca  Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca  Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca  Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa  Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55	100 s a 148 a 148 a 196 a 244
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc	100 s la 148 n la 196 ls la 244 /s la 292
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca  Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca  Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca  Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa  Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc  Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se	100 s la 148 n la 196 ls la 244 /s la 292
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se 60 65 70	100 s la 148 n la 196 la 244 /s la 292 er
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se 60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttct	100 s la 148 n la 196 la 244 /s la 292 er
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se 60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttctc Pro Phe Leu Ala Cys	100 s la 148 n la 196 la 244 /s la 292 er
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5	100 s a 148 a 148 a 196 a 244 y s 292 a 29
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se 60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttctc Pro Phe Leu Ala Cys 75  cgcagccgga gcaggtccct ttctagagat aggagaagag agagatcgct gtctcg	100 s la 148 n la 148 n la 148 s la 244 la 292 er la 347 ggag 407
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se 60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttctc Pro Phe Leu Ala Cys 75  cgcagccgga gcaggtccct ttctagagat aggagaagag agagatcgct gtctcgaagagagagagagagagagagagagagagagaga	100 s la 148 n la 148 n la 148 n la 148 la 244 la 292 er la 147 la 148 la 147 l
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5  1  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15  20  25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30  35  40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45  50  55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se  60  65  70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttctc Pro Phe Leu Ala Cys 75  cgcagccgga gcaggtccct ttctagagat aggagaagag agagatcgct gtctcga agaaatcaca agccgtcccg atccttctct aggtctcgta gtcgatttag gtcaaad aggaaataga agacagtttg caagagaagt ggtgtacagg aaattacttc atttgad	100 s la 148 n la 148 n la 148 n la 148 la 244 la 2
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se  60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagattctc Pro Phe Leu Ala Cys 75  cgcagccgga gcaggtcct ttctagagat aggagaaga agagatcgct gtctcga agaaatcaca agccgtcccg atccttctct aggtctcata agcttgtgc attttc	de 100 s la 148 la 148 la 196 ls la 244 ls la 292 ls la
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5	100 s la 148 n la 148
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se 60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttctc Pro Phe Leu Ala Cys 75  cgcagccgga gcaggtccct ttctagagat aggagaagag agagatcgct gtctcg agaaatcaca agccgtcccg atccttctct aggttcgta gtcgatttag gtcaaai aggaaataga agacagtttg caagagaagt ggtgtacaag aaattactc atttgad agtatgtaca gaaaattcaa gttttgtttg agacttcata agcttgtgc attttt tgttttagct gttcaaatct gtttgtctct tgaaacagtg acacaaaagt gtaatta atggtttgaa atggatcata cgaggcatgt aataccaaga attgttactt tacaatc	de 100 s la 148 la 148 la 196 ls la 244 ls la 292 ler la 347 lega 467 lega 467 lega 527 la 196 ls la 196 l
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se 60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttctc Pro Phe Leu Ala Cys 75  cgcagccgga gcaggtccct ttctagagat aggagaagag agagatcgct gtctcga agaaatcaca agccgtcccg atccttctct aggtctcgta gccgatttag gtcaaaa aggaaataga agacagtttg caagagaag ggtgtacagg aaattacttc atttgaa aggaaataga agacagtttg caagagaagt ggtgtacagg aaattacttc atttgaa agtatgtaca gaaaattcaa gtttgtttt agacttcata agcttggtcg attttt atggtttgaa atggatcata cgaggcatgt aataccaaga attgttactt tacaatc	de 100 s la 148 la 148 la 196 ls la 244 ls la 292 ler la 347 lega 467 lega 467 lega 527 lega 587 lett 647 gette 707 acet 767
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca ca Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro Hi  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca ca Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gl  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc ca Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile Hi  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Ly  45 50  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tc Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Se 60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttctc Pro Phe Leu Ala Cys 75  cgcagccgga gcaggtccct ttctagagat aggagaagag agagatcgct gtctcg agaaatcaca agccgtcccg atccttctct aggttcgta gtcgatttag gtcaaai aggaaataga agacagtttg caagagaagt ggtgtacaag aaattactc atttgad agtatgtaca gaaaattcaa gttttgtttg agacttcata agcttgtgc attttt tgttttagct gttcaaatct gtttgtctct tgaaacagtg acacaaaagt gtaatta atggtttgaa atggatcata cgaggcatgt aataccaaga attgttactt tacaatc	de 100 s la 148 la 148 la 196 ls la 244 ls la 292 ler la 347 lega 467 lega 467 lega 527 lega 587 lett 647 gette 707 acet 767

WO 99/31236 -64 - PCT/IB98/02122

aaattgaact aagatttact ttttttcca tagctgggat ataggctgca gctatagttg aacaagcagt ctttaaaaac tgctgtgaaa cacaggccat cagggaaaac gaaatgctgc actattaaat tagaggtttt tgaaaaatcc aactctcatc ctgggcagag gttgcctagt tggtatagaa tgttaagttt caagaaagtt tacctttgct ttaggtcgta agttccttat ttgattgccg tatatggata catggctgtt cgtgacattc tttatgtgca aatttgtgat ttcaaaaatg tcctgccagt ttaagggtac attgtagagc cgaactttga gttactgtgc aagatttttt ttcatgctgt catttgtaat atgttttgtg agaatccttg ggattaaagt tttggttaca gattaaaaaa aaaaa	887 947 1007 1067 1127 1187 1247 1272
<210> 88 <211> 804 <212> DNA	
<213> Homo sapiens	
<220> <221> CDS <222> 114734	
<221> sig_peptide	
<222> 114239 <223> Von Heijne matrix	
score 5.2 seq LLFDLVCHEFCQS/DD	
<221> polyA_signal <222> 768773	
<221> polyA_site <222> 793804	
<400> 88 ccaacaccag gaagagtetg aagagcagee agtgtttegg ettgtgeeet gtataettga	60
<400> 88  ccaacaccag gaagagtetg aagagcagee agtgtttegg ettgtgeeet gtataettga agetgeeaaa caagtaeggt agttetgaaa atceagaatg gettgatgtt tae atg  Met	60 116
ccaacaccag gaagagtotg aagagcagcc agtgtttcgg cttgtgccct gtatacttga agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg	
ccaacaccag gaagagtctg aagagcagcc agtgtttcgg cttgtgccct gtatacttga agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg Met cac att tta caa ctg ctt act aca gtg gat gat gga att caa gca att His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile -40 -35 -30 gta cat tgt cct gac act gga aaa gac att tgg aat tta ctt ttt gac Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp	116
ccaacaccag gaagagtctg aagagcagcc agtgtttcgg cttgtgccct gtatacttga agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg  Met  Cac att tta caa ctg ctt act aca gtg gat gat gga att caa gca att  His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile  -40 -35 -30  gta cat tgt cct gac act gga aaa gac att tgg aat tta ctt ttt gac  Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp  -25 -20 -15 -10  ctg gtc tgc cat gaa ttc tgc cag tct gat gat cca ccc atc att ctt	116 164
ccaacaccag gaagagtctg aagagcagcc agtgtttcgg cttgtgcct gtatacttga agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg  Met  Cac att tta caa ctg ctt act aca gtg gat gat gga att caa gca att  His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile  -40 -35 -30  gta cat tgt cct gac act gga aaa gac att tgg aat tta ctt ttt gac  Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp  -25 -20 -15 -10  ctg gtc tgc cat gaa ttc tgc cag tct gat gat cca ccc atc att ctt  Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile Leu  -5 1 5	116 164 212 260
ccaacaccag gaagagtctg aagagcagcc agtgtttcgg cttgtgcct gtatacttga agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg Met  Cac att tta caa ctg ctt act aca gtg gat gat gga att caa gca att His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile  -40 -35 -30  gta cat tgt cct gac act gga aaa gac att tgg aat tta ctt ttt gac  Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp  -25 -20 -15 -10  ctg gtc tgc cat gaa ttc tgc cag tct gat gat cca ccc atc att ctt  Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile Leu  -5 1 5  caa gaa cag aaa aca gtg cta gcc tct gtt ttt tca gtg ttg tct gcc  Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser Ala  10 15 20	116 164 212 260 308
ccaacaccag gaagagtctg aagagcagcc agtgtttcgg cttgtgcct gtatacttga agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg Met  cac att tta caa ctg ctt act aca gtg gat gat gga att caa gca att  His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile  -40 -35 -30  gta cat tgt cct gac act gga aaa gac att tgg aat tta ctt ttt gac  Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp  -25 -20 -15 -10  ctg gtc tgc cat gaa ttc tgc cag tct gat gat cca ccc atc att ctt  Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile Leu  -5 1 5  caa gaa cag aaa aca gtg cta gcc tct gtt ttt tca gtg ttg tct gcc  Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser Ala	116 164 212 260
ccaacaccag gaagagtctg aagagcagcc agtgtttcgg cttgtgcct gtatacttga agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg Met  Cac att tta caa ctg ctt act aca gtg gat gat gga att caa gca att His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile  -40 -35 -30  gta cat tgt cct gac act gga aaa gac att tgg aat tta ctt ttt gac  Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp  -25 -20 -15 -10  ctg gtc tgc cat gaa ttc tgc cag tct gat gat cca ccc atc att ctt  Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile Leu  -5 1 5  caa gaa cag aaa aca gtg cta gcc tct gtt ttt tca gtg ttg tct gcc  Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser Ala  10 15 20  atc tat gcc tca cag act gag caa gag tat cta aag ata gaa aaa gta  Ile Tyr Ala Ser Gln Thr Glu Gln Glu Tyr Leu Lys Ile Glu Lys Val  25 30 35  gat ctt cct cta att gac agc ctc att cgg gtc tta caa aat atg gaa	116 164 212 260 308
ccaacaccag gaagagtetg aagagcagce agtgtttegg ettgtgeeet gtataettga agetgeeaaa caagtaeggt agttetgaaa atecagaatg gettgatgtt tac atg Met  cac att tta caa etg ett act aca gtg gat gat gga att caa gca att  His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile  -40 -35 -30  gta cat tgt eet gae act gga aaa gae att tgg aat tta ett ttt gae  Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp  -25 -20 -15 -10  ctg gte tge cat gaa tte tge cag tet gat gat eea ee att ett  Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile Leu  -5 - 1 5  caa gaa cag aaa aca gtg eta gee tet gtt ttt tea gtg ttg tet gee  Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser Ala  10 ate tat gee tea cag act gag caa gag tat eta aag ata gaa aaa gta  Ile Tyr Ala Ser Gln Thr Glu Gln Glu Tyr Leu Lys Ile Glu Lys Val  25 - 30 - 35  gat ett eet ett att gae age ete att egg gte tta caa aat atg gaa  Asp Leu Pro Leu Ile Asp Ser Leu Ile Arg Val Leu Gln Asn Met Glu  40 - 45 - 50 - 55	116 164 212 260 308 356 404
ccaacaccag gaagagtctg aagagcagcc agtgtttcgg cttgtgcct gtatacttga agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg Met  cac att tta caa ctg ctt act aca gtg gat gat gga att caa gca att His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile  -40  -35  -30  gta cat tgt cct gac act gga aaa gac att tgg aat tta ctt ttt gac  Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp  -25  -20  -15  -10  ctg gtc tgc cat gaa ttc tgc cag tct gat gat cca ccc atc att ctt  Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile Leu  -5  caa gaa cag aaa aca gtg cta gcc tct gtt ttt tca gtg ttg tct gcc  Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser Ala  10  atc tat gcc tca cag act gag caa gag tat cta aag ata gaa aaa gta  Ile Tyr Ala Ser Gln Thr Glu Gln Glu Tyr Leu Lys Ile Glu Lys Val  25  gat ctt cct cta att gac agc ctc att cgg gtc tta caa aat atg gaa  Asp Leu Pro Leu Ile Asp Ser Leu Ile Arg Val Leu Gln Asn Met Glu  40  45  cag tgt cag aaa aaa cca gag aac tcg gca gag tct aac aca gag gaa  Gln Cys Gln Lys Lys Pro Glu Asn Ser Ala Glu Ser Asn Thr Glu Glu  60  65	116 164 212 260 308 356 404 452
ccaacaccag gaagagtetg aagagcagce agtgtttegg ettgtgeett gtatacttga agetgecaaa caagtaeggt agttetgaaa atecagaatg gettgatgtt tac atg Met  cac att tta caa etg ett act aca gtg gat gat gga att caa gca att His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile  -40  -35  gta cat tgt ect gac act gga aaa gac att tgg aat tta ett ttt gac  Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp  -25  -20  -15  -10  ctg gte tge cat gaa tte tge cag tet gat gat ecc ecc ate att ett  Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile Leu  -5  caa gaa cag aaa aca gtg eta gee tet gtt tt tea gtg ttg tet gee  Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser Ala  10  15  20  ate tat gee tea cag act gag caa gag tat eta aag ata gaa aaa gta  Ile Tyr Ala Ser Gln Thr Glu Gln Glu Tyr Leu Lys Ile Glu Lys Val  25  gat ett eet eta att gae age etc att egg gte tta eaa aat atg gaa  Asp Leu Pro Leu Ile Asp Ser Leu Ile Arg Val Leu Gln Asn Met Glu  45  cag tgt eag aaa aaa eca gag aac teg gea gag tet aac aca gag gaa  Gln Cys Gln Lys Lys Pro Glu Asn Ser Ala Glu Ser Asn Thr Glu Glu  60  65  70  act aaa agg act gat tta ace caa gat gat etc cae ttg aaa atc tta	116 164 212 260 308 356 404
ccaacaccag gaagagtctg aagagcagcc agtgtttcgg cttgtgcct gtatacttga agctgccaaa caagtacggt agttctgaaa atccagaatg gcttgatgtt tac atg Met  cac att tta caa ctg ctt act aca gtg gat gat gga att caa gca att His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala Ile  -40  -35  -30  gta cat tgt cct gac act gga aaa gac att tgg aat tta ctt ttt gac  Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp  -25  -20  -15  -10  ctg gtc tgc cat gaa ttc tgc cag tct gat gat cca ccc atc att ctt  Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile Leu  -5  caa gaa cag aaa aca gtg cta gcc tct gtt ttt tca gtg ttg tct gcc  Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser Ala  10  atc tat gcc tca cag act gag caa gag tat cta aag ata gaa aaa gta  Ile Tyr Ala Ser Gln Thr Glu Gln Glu Tyr Leu Lys Ile Glu Lys Val  25  gat ctt cct cta att gac agc ctc att cgg gtc tta caa aat atg gaa  Asp Leu Pro Leu Ile Asp Ser Leu Ile Arg Val Leu Gln Asn Met Glu  40  45  cag tgt cag aaa aaa cca gag aac tcg gca gag tct aac aca gag gaa  Gln Cys Gln Lys Lys Pro Glu Asn Ser Ala Glu Ser Asn Thr Glu Glu  60  65	116 164 212 260 308 356 404 452

·	
90 95 100	
aag gag acg gtg gct cag gga gta aag gaa ggc cag ttg agc aaa cag	596
Lys Glu Thr Val Ala Gln Gly Val Lys Glu Gly Gln Leu Ser Lys Gln	
105 110 115 aag tgt tcc tct gca ttt caa aac ctt ctt cct ttc tat agc cct gtg	644
Lys Cys Ser Ser Ala Phe Gln Asn Leu Leu Pro Phe Tyr Ser Pro Val	٠
120 125 130 135	
gtg gaa gat ttt att aaa atc cta cgt gaa gtt gat aag gcg ctt gct	692
Val Glu Asp Phe Ile Lys Ile Leu Arg Glu Val Asp Lys Ala Leu Ala	
140 145 150	
gat gac ttg gaa aaa aac ttc cca agt ttg aag gtt cag act	734
Asp Asp Leu Glu Lys Asn Phe Pro Ser Leu Lys Val Gln Thr	
155 160 165	
taaaacctga attggaatta cttctgtaca agaaataaac tttatttttc tcactgaca	
aaaaaaaaa	804
•	
212 22	
<210> 89 <211> 802	
<211> 602 <212> DNA	
<213> Homo sapiens	
1223 Nono Supremo	
<220>	
<221> CDS	
<222> 199801	
·	
<221> polyA_signal	
<222> 780785	
<221> polyA_site	
<221> polyA_site <222> 791802	
<222> 791802	
<222>, 791, .802 <400> 89	ag 60
<222> 791802  <400> 89  agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag	ag 60
<pre>&lt;222&gt; 791.802 &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtgtgt tggaaatcgc tctcgctttg ccaagggaga ctatttac</pre>	ga 120
<222> 791.802  <400> 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg	ga 120 cc 180
<pre>&lt;222&gt; 791.802 &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231
<222> 791802  <400> 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc Met Gln Val Ala Leu Lys Glu Asp Leu Asp Ala	ga 120 cc 180 231
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231
<pre>&lt;222&gt; 791.802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327
<pre>&lt;222&gt; 791802  &lt;400&gt; 89  agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 3375
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 3375
<pre>&lt;222&gt; 791802  &lt;400&gt; 89  agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 3375
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 375 c 423 471
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 375 c 423 471
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgggc tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat</pre>	ga 120 cc 180 231 279 327 375 423 471
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 375 423 471 1 519
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaaagggaga ctattac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 375 423 471 1 519
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggagaa ctattac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 375 423 471 1 519
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaaagggaga ctattac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 375 423 471 1 519 n 567
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231 279 327 375 423 471 1 519 n 567
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231  279  327  375  423  471  519  567
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact ctgagtccag ctccgaag gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg ccaagggaga ctatttac tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc ttgctgcctg tgttgtgg tgtgttggct tggtgtgg atg cag gtt gct ctc aag gag gat ctg gat gcc</pre>	ga 120 cc 180 231  279  327  375  423  471  519  567

Asp Glu His Lys Lys Thr Met Glu Leu Leu Gln Ser Asp Met Asn Gln 125 130 135	
cac ttc ttg aag gag act cct gga agc aac cag atc att ccg tca cct	663
His Phe Leu Lys Glu Thr Pro Gly Ser Asn Gln Ile Ile Pro Ser Pro	
· · · · · · · · · · · · · · · · · · ·	
= **	211
tca gcc aca tca gaa ctt gac aat aaa acc cac agt gag aat ttg aaa	711
Ser Ala Thr Ser Glu Leu Asp Asn Lys Thr His Ser Glu Asn Leu Lys	
160 165 170	
cag atg ggt gat aga tot god act otg aaa aga dag tot ttg gad daa	75 <b>9</b>
Gln Met Gly Asp Arg Ser Ala Thr Leu Lys Arg Gln Ser Leu Asp Gln	
175 180 185	
	802
gtc acc aac aga aca gat aca gta aaa atc caa aaa aaa aaa a	802
Val Thr Asn Arg Thr Asp Thr Val Lys Ile Gln Lys Lys	
190 195 200	
01000	
<210> 90	
<211> 1490	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 381174	
<221> sig_peptide	
<222> 38148	
<223> Von Heijne matrix	
score 7.3	
seq LLSACLVTLWGLG/EP	
-	
<221> polyA_signal	
<222> 14521457	
<222> 1432143/	
<221> polyA_site	
<222> 14781490	
<400> 90	
tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg	55
Met Pro His Ser Ser Leu	
-35	102
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc	103
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc	103
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala	103
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20	
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20  ttg qtt ctq ctq agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag	103
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu	
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu -15 -10 -5	151
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu -15 -10 -5	
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu -15 -10 -5 1 cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg	151
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu -15 -10 -5 1 cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu	151
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu -15 -10 -5 1 cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu 5	151
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  cag ctg gga ctg ctg ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg	151
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  cag ctg gga ctg ctg ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg	151
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc ttgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  10  15  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu	151
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30	151
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30  cqc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg	151 199 247
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc ttg ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg	151 199 247
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35	151 199 247 295
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  45  qcc ttg ctg ctg ctg ctg tcc ctc cgc cgt ggg gcc ctg ttg ctg c	151 199 247
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  45  qcc ttg ctg ctg ctg ctg tcc ctc cgc cgt ggg gcc ctg ttg ctg c	151 199 247 295
cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  10  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  45  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	151 199 247 295
Cat       cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc         His       Pro       Ser Ile       Pro       Cys       Pro       Arg       Gly       His       Gly       Ala       Gln       Lys       Ala       Ala         1       -30       -25       -20       -20       -20       -10       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -5       1       -20       -5       1       -10       -5       -10       -5       -10       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20	151 199 247 295
Cat       cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc         His       Pro       Ser Ile       Pro       Cys       Pro       Arg       Gly       His       Gly       Ala       Gln       Lys       Ala       Ala         -30       -25       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20 <t< td=""><td>151 199 247 295</td></t<>	151 199 247 295
Cat       cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc         His       Pro       Ser Ile       Pro       Cys       Pro       Arg       Gly       His       Gly       Ala       Gln       Lys       Ala       Ala         1       -30       -25       -20       -20       -20       -10       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -5       1       -20       -5       1       -10       -5       -10       -5       -10       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20       -20	151 199 247 295

				70					75					80		
tqq	atg	ctt	gcc	ctc	ctg	ggc	ctc	tcg	cag	gca	ctg	aac	atc	ctc	ctg	439
Trp	Met	Leu	Ala	Leu	Leu	Gly	Leu	Ser	Gln	Ala	Leu	Asn	Ile	Leu	Leu	
			85					90					95			
ggc	ctc	aag	ggc	ctg	gcc	cca	gct	gag	atc	tct	gca	gtg	tgt	gaa	aaa	487
Gly	Leu		Gly	Leu	Ala	Pro		Glu	Ile	Ser	Aia		Cys	GIU	Lys	
		100					105	cta	<b>~~</b>	+~~	F C 2	110	tac	arc	ara .	535
999	aat Asn	מלכ	aac	grg	gcc	Uic	999	Lau	NI a	Trn	Ser	Tyr	Tyr	Tle	G) v	333
Gly	115	FIIC	Mail	VAI	AIG	120	Gry	пси	714	115	125	- ] -	-1-		027	
tat	ctg	caa	cta	atc	cta		αaα	ctc	caq	qcc		att	cga	act	tac	583
Tvr	Leu	Arg	Leu	Ile	Leu	Pro	Glu	Leu	Gln	Ala	Arg	Ile	Arg	Thr	Tyr	
130		_			135					140	_				145	
aat	cag	cat	tac	aac	aac	ctg	cta	cgg	ggt	gca	gtg	agc	cag	cgg	ctg	631
Asn	Gln	His	Tyr	Asn	Asn	Leu	Leu	Arg	Gly	Ala	Val	Ser	Gln	Arg	Leu	
				150					155					160		
tat	att	ctc	ctc	cca	ttg	gac	tgt	<b>999</b>	gtg	cct	gat	aac	ctg	agt	atg	679
Tyr	Ile	Leu		Pro	Leu	Asp	Cys		Val	Pro	Asp	Asn	Leu	ser	Mec	
			165					170					175	300	cat	. 727
gct	gac	ccc	aac	att	cgc	ttc	ctg	gat	aaa	ctg	CCC	cag	Cla	Thr	gg c	141
Ala	Asp		Asn	Ile	Arg	Pne		Asp	Lys	Leu	PIO	190	GIII	IIII	GLY	
	cgt	180				~~ - t	185	~++	tac	200	220		atc	tat	gag	775
gac	Arg	gcc	ggc	atc	aag	yat Non	223	Val	Tur	Ser	Acn	Ser	Tle	Tvr	Glu	
Asp	195	AIA	GIY	116	гуя	200	Arg	Val	171	JGI	205	001		-1-		
c++	ctg	a a a	220	aaa	can		aca	aac	acc	tat		cta	ааа	tac	qcc	823
Len	Leu	Glu	Agn	61v	Gln	Ara	Ala	Glv	Thr	Cvs	Val	Leu	Glu	Tyr	Ala	
210	пец	GIU	M311	Gly	215	y		017		220				•	225	
	ccc	rta	cag	act		ttt	acc	atq	tca		tac	agt	caa	gct	ggc	871
Thr	Pro	Leu	Gln	Thr	Leu	Phe	Ala	Met	Ser	Gln	Tyr	Ser	Gln	Ala	Gly	
				230			,		235		_			240		
ttt	agc	caa	qaq	qat	agg	ctt	gag	cag	gcc	aaa	ctc	ttc	tgc	cgg	aca	919
Phe	Ser	Arg	Glu	Asp	Arg	Leu	Glu	Gln	Ala	Lys	Leu	Phe	Cys	Arg	Thr	
			245					250					255			
ctt	gag	gac	atc	ctg	gca	gat	gcc	cct	gag	tct	cag	aac	aac	tgc	cgc	967
Leu	Glu	Asp	Ile	Leu	Ala	Asp			Glu	Ser	Gln	Asn	Asn	Cys	Arg	
		260					265					270				1015
ctc	att	gcc	tac	cag	gaa	cct	gca	gat	gac	agc	ago	ttc	tcg	ctg	tcc	1015
Leu		Ala	Tyr	Gln	Glu			Asp	Asp	Ser	Ser	Pne	Ser	Leu	Ser	
	275					280					285		<b>~~~</b>	att	200	1063
cag	gag	gtt	ctc	cgg	cac	ctg	cgg	cag	gag	gaa	Tue	, Glu	Glu	Val	acc Thr	
	Glu	Val	Leu	Arg			Arg	GIII	Glu	300	, mys	, 010	. Olu	, ,,,,	. Thr 305	
290					295			. ata				tee	. aco	ato		1111
gtg	ggc	agc	ttg	aag	The	Car	. gcg	val	Dro	Ser	Thi	Ser	Thr	Met	tcc Ser	
vaı	GIY	ser	Leu	310		361	AT.	val	315	, 001 i	• • • • •			320	)	
	~~~	cet	G2G	Ctc	ctc	cto	agt	gga			aaa	2 000	cto	: cct	ctc	1159
Gla	Glu	220	Glu	LAN	Leu	Lev	Ser	· Glv	Met	: Glv	/ Lv	s Pro	Lev	Pro	Leu	
GIII	Giu	PIO	325		. 500			330		1	•		335	5		
cac	асп	gat			tga	gaco	cag			agg d	caq	agect	to ca	agtg	gtctc	1214
	Thr					. 5		33			-	_				
9		340			•											
caa	acct	cta	gact	gaac	iac t	ctct	tcad	gt go	gctga	aatgi	t cc	agca	gagc	tat	ttccttc	1274
cac	aggg	aac	ctte	icado	oa a	aaat	ccad	ag ac	cttga	acat	c ::	aaga	tgcg	CCC	tgtcccc	1334
tta	aacc	agt	catt	tcc	cct o	tcte	gage	ct cg	ggtgi	tctt	c aa	cctg	tgaa	atg	ggatcat	1394
aat	cact	acc	ttac	ctc	ct d	acq	gttg	tt gi	gag	gact	g ag	tgtg	tgga	agt	ttttcat	1454
aaa	cttt	gga	tact	agt	ata (tta	aaaa	aa aa	aaaa	a						1490
				. د	•											

<210> 91 <211> 361

```
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 26..361
<221> polyA_site
<222> 350..361
                                                                      52
tegagaaget geceettage caace atg eeg tet gag ggt ege tge tgg gag
                            Met Pro Ser Glu Gly Arg Cys Trp Glu
acc ttg aag gcc cta cgc agt tcc gac aaa ggt cgc ctt tgc tac tac
                                                                     100
Thr Leu Lys Ala Leu Arg Ser Ser Asp Lys Gly Arg Leu Cys Tyr Tyr
                    15
                                        20
ege gae tgg etg etg egg ege gag gat gtt tta gaa gaa tgt atg tet
                                                                     148
Arg Asp Trp Leu Leu Arg Arg Glu Asp Val Leu Glu Glu Cys Met Ser
               30
                                                                     196
ctt ccc aag cta tct tct tat tct gga tgg gtg gta gag cac gtc cta
Leu Pro Lys Leu Ser Ser Tyr Ser Gly Trp Val Val Glu His Val Leu
                                50
ccc cat atg cag gag aac caa cct ctg tct gag act tcg cca tcc tct
                                                                     244
Pro His Met Gln Glu Asn Gln Pro Leu Ser Glu Thr Ser Pro Ser Ser
                                                70
                            65
                                                                     292
acg tea get tea gee eta gat caa ece tea tit git eee aaa tet eet
Thr Ser Ala Ser Ala Leu Asp Gln Pro Ser Phe Val Pro Lys Ser Pro
                                            85
                       80
gac gca agc tct gcc ttt tcc cca gcc tcc cct gca aca cca aat gga
                                                                      340
Asp Ala Ser Ser Ala Phe Ser Pro Ala Ser Pro Ala Thr Pro Asn Gly
                                        100
90
                                                                      361
acc aag ggc aaa aaa aaa aaa
Thr Lys Gly Lys Lys Lys
                110
<210> 92
<211> 605
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 3..131
<221> polyA site
<222> 591..605
<400> 92
ca too oft occ cag got tha tgg the cag the the tac cae tot gga
                                                                        47.
   Ser Leu Pro Gln Ala Leu Trp Phe Gln Phe Phe Tyr His Ser Gly
                                        10
age tee eta gaa tet eet gga atg ett aat gga eet tte eag eac ega
                                                                        95
Ser Ser Leu Glu Ser Pro Gly Met Leu Asn Gly Pro Phe Gln His Arg
                                     25
                . 20
                                                                       141
 aat tca aga att atg act cat cgg tca gca gaa aag tgaggatacc
 Asn Ser Arg Ile Met Thr His Arg Ser Ala Glu Lys
             35 ,
 ttttcctaac ctacctgctt cccctgcagt ttcctcacaa tcttactctt tatattttag
                                                                       201
catatgtagc ttctcaggat gttaattctg ttctctctgt gttggtgtct gagcacccag
                                                                       261
```

321

aaggtagagc caggggcact tataaaccag gagcattatt tgacaggcac ttaagaaaga

cactggctac gtaatccag cactttggga ggctgaggcg gatggatcac atgaggtcag gagttcgaga ccagcttggc cagcatggtg aaaccctgtc tctactaaaa atacaaaaat tagctgggtg tggttgcaca cgcctgtaat cccagctacc tgggaggctg aggcaggaga atcgcttgaa cttgggaggc ggaggttgca gtgagcctag attttgccat tgcactccag cctgggtgac aagggcgaaa ctccatccca aaaaaaaaaa	381 441 501 561 605
<210> 93 <211> 591 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 33185	
<221> sig_peptide <222> 3380 <223> Von Heijne matrix score 3.7 seq IALTLIPSMLSRA/AG	
<pre><221> polyA_signal <222> 570575</pre>	
<221> polyA_site <222> 586591	
<400> 93 caatcttctc agcttataac cgtctttccc tt atg cta agg ata gcc ctt aca Met Leu Arg Ile Ala Leu Thr	53
ctc atc cca tct atg ctg tca agg gct gct ggt tgg tgc tgg tac aag Leu Ile Pro Ser Met Leu Ser Arg Ala Ala Gly Trp Cys Trp Tyr Lys -5 1 5	101
gag ccc act cag cag ttt tct tac ctt tgc ctg ccc tgc ctt tca tgg Glu Pro Thr Gln Gln Phe Ser Tyr Leu Cys Leu Pro Cys Leu Ser Trp 10 15 20	149
aat aag aaa ggc aac gtt ttg cag ctt cca aat ttc tgaagaaact Asn Lys Lys Gly Asn Val Leu Gln Leu Pro Asn Phe 25 30 35	199
aatotoagat tggcagttaa agtcaaaatg ttgccaaata tttattcctt ttgcctaagt	259
tragetacce ageticating cittitate transfer gaetetrag agetication	319
tcaaaagaac aatgagaaca tttgctttgc tttctgctga atccctaatc tcaacaatct	375 43
atacetggae tgtecagtte tecteetgtg etatettete ttetatecaa gtagaatgta	49
tgccaggage teetteecte tageaattte tactaaaatg teeaagtaga atgttteett ttacaateaa attactgtat ttattaattt getagaatee agtaaateat tttggtaget	55
ctggctgtgc tatcaataaa aagatgaaag caaaaa	59
<210> 94	
<211> 94 <211> 1150	
<212> DNA	

<220>
<221> CDS
<222> 184..915

WO 99/31236 -70- PCТ/IB98/02122

<221> sig peptide <222> 184..237 <223> Von Heijne matrix score 3.5 seg LLGLELSEAEAIG/AD <221> polyA_signal <222> 1119..1124 <221> polyA site <222> 1139..1150 <400> 94 cggatttgac gatggtgttc ggtcttgaat ggaaatgtag tcttaggcca gtcttaggtt tttgaacagg atagtaggta tccggagtcg attgagggcc agagcaggca ctggggttcg 120 gatoctgggc aaagtttocc acgttgaggg totcgaggac gootagatot otttoccagg 180 gcc atg gcg aac ccg aag ctg ctg gga ctg gag cta agc gag gcg gag 228 Met Ala Asn Pro Lys Leu Leu Gly Leu Glu Leu Ser Glu Ala Glu -10 - 15 gcg atc ggt gct gat tcg gcg cga ttt gag gag ctg ctg ctg cag gcc 276 Ala Ile Gly Ala Asp Ser Ala Arg Phe Glu Glu Leu Leu Gln Ala 5 tcg aag gag ctc cag caa gcc cag aca acc aga cca gaa tcg aca caa 324 Ser Lys Glu Leu Gln Gln Ala Gln Thr Thr Arg Pro Glu Ser Thr Gln 15 20 atc cag cct cag cct ggt ttc tgc ata aag acc aac tcc tcg gaa ggg 372 Ile Gln Pro Gln Pro Gly Phe Cys Ile Lys Thr Asn Ser Ser Glu Gly 35 40 aag gtt ttc atc aac atc tgc cac tcc ccc tct atc cct ccc gcc 420 Lys Val Phe Ile Asn Ile Cys His Ser Pro Ser Ile Pro Pro Pro Ala 50 gac gtg acc gag gag gag ctg ctt cag atg cta gag gag gac caa gct 468 Asp Val Thr Glu Glu Glu Leu Leu Gln Met Leu Glu Glu Asp Gln Ala 70 516 ggg ttt cgc atc ccc atg agt ctg gga gag cct cat gca gaa ctg gat Gly Phe Arg Ile Pro Met Ser Leu Gly Glu Pro His Ala Glu Leu Asp 80 85 gca aaa ggc cag gga tgt acc gcc tac gac gta gct gtc aac agc gac 564 Ala Lys Gly Gln Gly Cys Thr Ala Tyr Asp Val Ala Val Asn Ser Asp 100 105 612 tto tac egg agg atg cag aac age gat tto ttg egg gag etc gtg atc Phe Tyr Arg Arg Met Gln Asn Ser Asp Phe Leu Arg Glu Leu Val Ile . 120 110 115 acc atc gcc agg gag ggc ctt gag gac ata tac aac ttg cag ctg aat 660 Thr Ile Ala Arg Glu Gly Leu Glu Asp Ile Tyr Asn Leu Gln Leu Asn 130 135 ccg gaa tgg cgc atg atg aag aac cgg cca ttc atg ggc tcc atc tcg 708 Pro Glu Trp Arg Met Met Lys Asn Arg Pro Phe Met Gly Ser Ile Ser 150 cag cag aac atc cgc tcg gag cag cgt cct cgg atc cag gag ctg ggg 756 Gln Gln Asn Ile Arg Ser Glu Gln Arg Pro Arg Ile Gln Glu Leu Gly 165 170 804 gac ctg tac acg ccc gcc ccc ggg aga gct gag tca ggg cct gaa aag Asp Leu Tyr Thr Pro Ala Pro Gly Arg Ala Glu Ser Gly Pro Glu Lys 185 180 852 cet cae etg aac etg tgg etg gaa gee eee gae ete ete ttg gee gaa Pro His Leu Asn Leu Trp Leu Glu Ala Pro Asp Leu Leu Ala Glu 200 195 gtt gac etc ecc aaa etg gat gga gee etg ggg etg teg etg gag atc 900 Val Asp Leu Pro Lys Leu Asp Gly Ala Leu Gly Leu Ser Leu Glu Ile 215 210 ggg aga acc gcc tgg tgatgggggg cccccagcag ctgtatcatc tagacgctta 955 WO 99/31236 -71- PCT/IB98/02122

	Arg		Ala 225	Trp												
atta	atgg agat	cg c tg g gt g	agat ccat gaga	gccg agag	c tt	ctgc	ggt	gcct	tctt	ga t	cage	gtgt	c to	ctto	aagca gtgct tgcc	1015 1075 1135 1150
<210 <211 <212 <213	> 15	A	apie	ns												
	> > CD > 58	s	15													
<222		15 n He ore	9 ijne 4			DP										
	> po > 14	lyA_	sign	al												
	> po > 15		•													
	> 95						~~~		2202	++c	aaas	actt	ct t	cago	aa	57
atq	gag	aga	ggc	ctg	aaa	tca	gca	gac	cct	cgg	ggga gat	ggc	acc	ggt	tac	105
				-30					-25		Asp			-20		
act Thr	Gly	tgg Trp	gca Ala	ggt Gly	att Ile	gct Ala	gtg Val	ctt	tac	tta				rat		
ttt			-15					-10	Tyr	Leu	His	ctt Leu	Tyr -5	Asp	Val	153
Phe	Gly	gac Asp	-15 cct Pro	gcc Ala	tac Tyr	cta Leu	cag	-10 tta	Tyr gca	Leu cat	His ggc Gly	Leu tat	Tyr -5 gta	Asp aag	Val caa	201
Phe agt Ser	Gly	Asp 1 aac	cct Pro	Ala tta	Tyr acc Thr	cta Leu 5 aag	cag Gln	-10 tta Leu tcc	Tyr gca Ala atc	cat His acc Thr	His	Leu tat Tyr	Tyr -5 gta Val tgt	aag Lys 999	caa Gln gat Asp	
Phe agt Ser 15	Gly ctg Leu	Asp 1 aac Asn	cct Pro tgc Cys	Ala tta Leu gca Ala	Tyr acc Thr 20	cta Leu 5 aag Lys	cag Gln cgc Arg	-10 tta Leu tcc Ser	Tyr gca Ala atc Ile cta Leu	cat His acc Thr 25 tat	ggc Gly 10 ttc	tat Tyr ctt Leu	Tyr -5 gta Val tgt Cys atg	Asp aag Lys ggg Gly aac Asn	caa Gln gat Asp 30	201
Phe agt Ser 15 gca Ala	Gly ctg Leu ggc Gly	Asp 1 aac Asn ccc Pro	cct Pro tgc Cys ctg Leu gca Ala	Ala tta Leu gca Ala 35	Tyr acc Thr 20 gtg Val	cta Leu 5 aag Lys gcc Ala	cag Gln cgc Arg gct Ala	-10 tta Leu tcc Ser gtg Val aca Thr	Tyr gca Ala atc Ile cta Leu 40 cgg	cat His acc Thr 25 tat Tyr	ggc Gly 10 ttc Phe	tat Tyr ctt Leu aag Lys	Tyr -5 gta Val tgt Cys atg Met cta Leu	Asp aag Lys ggg Gly aac Asn 45 aat	caa Gln gat Asp 30 aat Asn	201
Phe agt Ser 15 gca Ala gag Glu att	Cly Ctg Leu Ggc Gly aag Lys	Asp 1 aac Asn ccc Pro cag Gln cct Pro	cct Pro tgc Cys ctg Leu gca Ala 50 cat	Ala tta Leu gca Ala 35 gaa Glu	Tyr acc Thr 20 gtg Val gat Asp	cta Leu 5 aag Lys gcc Ala tgc Cys	cag Gln cgc Arg gct Ala atc Ile gaa Glu	-10 tta Leu tcc Ser gtg Val aca Thr 55 atg	Tyr gca Ala atc Ile cta Leu 40 cgg Arg	cat His acc Thr 25 tat Tyr cta Leu	ggc Gly 10 ttc Phe cat His att Ile	tat Tyr ctt Leu aag Lys cac His	Tyr -5 gta Val tgt Cys atg Met cta Leu 60 ata	Asp aag Lys ggg Gly aac Asn 45 aat Asn	caa Gln gat Asp 30 aat Asn	201 249 297
Phe agt Ser 15 gca Ala gag Glu att Ile	Gly ctg Leu ggc Gly aag Lys gat Asp tat Tyr	Asp 1 aac Asn ccc Pro cag Gln cct Pro 65	cct Pro tgc Cys ctg Leu gca Ala 50 cat His	Ala tta Leu gca Ala 35 gaa Glu gct Ala	Tyr acc Thr 20 gtg Val gat Asp cca Pro	cta Leu 5 aag Lys gcc Ala tgc Cys aat Asn gtc Val	cag Gln cgc Arg gct Ala atc Ile gaa Glu 70 aat	-10 tta Leu tcc Ser gtg Val aca Thr 55 atg Met	Tyr gca Ala atc Ile cta Leu 40 cgg Arg ctc Leu aac	cat His acc Thr 25 tat Tyr cta Leu tat Tyr	His ggc Gly 10 ttc Phe cat His att Ile ggg Gly	tat Tyr ctt Leu aag Lys cac His cga Arg 75 gtg	Tyr -5 gta Val tgt Cys atg Met cta Leu 60 ata Ile gaa	Asp aag Lys Gly aac Asn 45 aat Asn Gly	caa Gln gat Asp 30 aat Asn aag Lys	201 249 297 345
Phe agt Ser 15 gca Ala gag Glu att Ile atc	Gly ctg Leu ggc Gly aag Lys gat Asp tat Tyn	Asp 1 aac Asn ccc Pro cag Gln cct Pro 65 gct Ala	cct Pro tgc Cys ctg Leu gca Ala 50 cat His ctt Leu	Ala tta Leu gca Ala 35 gaa Glu gct Ala ctt Leu	Tyr acc Thr 20 gtg Val gat Asp cca Pro ttt	cta Leu 5 aag Lys gcc Ala tgc Cys aat Asn gtc Val 85 cag Gln	cag Gln cgc Arg gct Ala atc Ile gaa Glu 70 aatt Asn	-10 tta Leu tcc Ser gtg Val aca Thr 55 atg Met aag Lys	Tyr gca Ala atc Ile cta Leu 40 cgg Arg ctc Leu aac Asn	Leu cat His acc Thr 25 tat Tyr cta Leu tat Tyr ttt Phe aca	His ggc Gly 10 ttc Phe cat His att Ile ggg Gly gga Gly 90 att Ile	Leu tat Tyr ctt Leu aag Lys cac His cga Arg 75 gtg Val	Tyr -5 gta Val tgt Cys atg Met cta Leu 60 ata Ile gaa Glu acc	Asp aag Lys ggg Gly aac Asn 45 aat Asn ggc Gly aag Lys	caa Gln gat Asp 30 aat Asn aag Lys tac Tyr	201 249 297 345 393

WO 99/31236 -72 - PCT/IB98/02122

tat	gaa	tgg	tac	cag	gaa	tat	tat	gta	999	gct	gct	cat	ggc	ctg	gct	585
Tyr	Glu	Trp	Tyr	Gln	Glu	Tyr	Tyr	Val	Gly	Ala	Ala	His	Gly	Leu	Ala	
_		_	130			•		135					140		•	
gga	att	tat	tac	tac	ctg	atg	cag	CCC	agc	ctt	caa	gtg	agc	caa	9 99	633
Gly	Ile	Tyr	Tyr	Tyr	Leu	Met	Gln	Pro	Ser	Leu	Gln	Val	Ser	Gln	Gly	
•		145	•				150					155				
aag	tta	cat	agt	ttg	gtc	aag	ccc	agt	gta	gac	tac	gtc	tgc	cag	ctg	681
Lys	Leu	His	Ser	Leu	Val	Lys	Pro	Ser	Val	Asp	Tyr	Val	Cys	Gln	Leu	
	160					165					170					
aaa	ttc	cct	tct	ggc	aat	tac	cct	cca	tgt	ata	ggt	gat	aat	cga	gat	729
Lys	Phe	Pro	Ser	Gly	Asn	Tyr	Pro	Pro	Cys	Ile	Gly	Asp	Asn	Arg	Asp	
175					180					185					190	
					tgc											777
Leu	Leu	Val	His	Trp	Cys	His	Gly	Ala	Pro	Gly	Val	Ile	Tyr	Met	Leu	
				195					200					205		
atc	cag	gcc	tat	aag	gta	ttc	aga	gag	gaa	aag	tat	ctc	tgt	gat	gcc	825
Ile	Gln	Ala	Tyr	Lys	Val	Phe	Arg	Glu	Glu	Lys	Tyr	Leu	Cys	Asp	Ala	
			210					215					220			
tat	cag	tgt	gct	gat	gtg	atc	tgg	caa	tat	999	ttg	ctg	aag	aag	gga	873
Tyr	Gln	Cys	Ala	Asp	Val	Ile	Trp	Gln	Tyr	Gly	Leu	Leu	Lys	Lys	Gly	
		225					230					235				
tat	999	ctg	tgc	cac	ggt	tct	gca	999	aat	gcc	tat	gcc	ttc	ctg	aca	921
Tyr	Gly	Leu	Cys	His	Gly	Ser	Ala	Gly	Asn	Ala	Tyr	Ala	Phe	Leu	Thr	
	240					245					250					
					cag											969
Leu	Tyr	Asn	Leu	Thr	Gln	Asp	Met	Lys	Tyr	Leu	Tyr	Arg	Ala	Cys	Lys	
255					260					265					270	
ttt	gct	gaa	tgg	tgc	tta	gag	tat	gga	gaa	cat	gga	tgc	aga	aca	cça	1017
Phe	Ala	Glu	Trp	Cys	Leu	Glu	Tyr	Gly	Glu	His	Gly	Cys	Arg	Thr	Pro	
				275					280					285		
gac	acc	cct	ttc	tct	ctc	ttt	gaa	gga	atg	gct	999	aca	ata	tat	ttc	1065
Asp	Thr	Pro	Phe	Ser	Leu	Phe	Glu	Gly	Met	Ala	Gly	Thr		Tyr	Phe	
			290					295					300			
ctg	gct	gac	ctg	cta	gtc	CCC	aça	aaa	gcc	agg	ttc	cct	gca	ttt	gaa	1113
Leu	Ala	Asp	Leu	Leu	Val	Pro	Thr	Lys	Ala	Arg	Phe		Ala	Phe	Glu	
		305					310					315				
ctc	tgaa	aagga	ata 9	gcat	gcca	cc t	gcaa	ctca	c tg	catg	accc	ttt	ctgt	ata		1166
Leu																
ttc	aaac	ca a	agct	aagt	gc t	tccg	ttgc	t tt	ccaa	ggaa	aca	aaga	gtc	aaac	tgtgga	1226
ctt	gatt	ttg 1	tag	cttt	tt t	caga	attt	a tc	tttc	attc	agt	tccc	ttc	catt	atcatt	1286
tact	tttt	act 1	taga	agta	tc c	aagg	aagt	c tt	ttaa	cttt	aat	ttcc	att	tctt	cctaaa	1346
ggga	agagi	tga g	gtga	tatg	ta c	agtg	tttt	g ag	attg	tata	cat	atat	tcc	agaa	cttgga	1406
gga	aatc	tta 1	ttta	agtt	ta t	gaat	ataa	с са	tctg	ttac	tgt	tcta	aaa	atgt	ttaaaa	1466
gaaa	actc	aat a	acag	ataa	ag a	taaa	tatg	t ga	ctat	taaa	aaa	aaaa				1513

```
<210> 96

<211> 417

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 327..416

<221> polyA_site

<222> 404..417
```

<400> 96
tgttttgagg tgttggcatt cttcgctgat ttggctgttc ccaatgttta cattatttaa 60
tcttgcaaaa atggttctgt gcacttggat gtgaaatgct gtccagtttt attttttta 120

tgttgttatc cttggatgta caaaaaattc agaaaatgat ctctgtagat attctgtttt	180
artttggtca totttagaag ttatcaggaa tgtgtttaaa acaagaagag aacttttota	240
aggaatgata catagaaaag attttatttt aaaatgagtt gtaaagcttg tgtttctttg	300
ttgctgcaag ctatctgccc aagtta atg caa atg gac aca ttt ttt atg tca	353
Met Gln Met Asp Thr Phe Phe Met Ser	
1 5	
gaa aaa cac aca cac aca cac aca cat ata cac aca cac aca cga aaa	401
Glu Lys His Thr His Thr His Thr His Ile His Thr His Thr Arg Lys	
10 15 20 25	
aca aaa aaa aaa a	417
Thr Lys Lys Lys	
30	
<210> 97	
<211> 603	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 63398	
·	
<221> sig_peptide	
<222> 63206	
<223> Von Heijne matrix	
score 4.9	
seq PSLAAGLLFGSLA/GL	
5 5 4 · D - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	
· 400> 97	
<400> 97 ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	60
ggggcetteg tgagaceggt gcaggeetgg ggtagtetee tgtetggaca gagaagagaa	60 107
ggggcetteg tgagaceggt gcaggeetgg ggtagtetee tgtetggaca gagaagagaa	
gggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagaaa aa atg cag gac act ggc tca gta gtg cct ttg cat tgg ttt ggc ttt Met Gln Asp Thr Gly Ser Val Val Pro Leu His Trp Phe Gly Phe	107
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107
gggggcetteg tgagaceggt geaggeetgg ggtagtetee tgtetggaca gagaagagaa aa atg cag gac act gge tea gta gtg cet ttg cat tgg ttt gge ttt Met Gln Asp Thr Gly Ser Val Val Pro Leu His Trp Phe Gly Phe -45 -40 -35 gge tac gca gca ctg gtt gct tct ggt ggg atc att ggc tat gta aaa Gly Tyr Ala Ala Leu Val Ala Ser Gly Gly Ile Ile Gly Tyr Val Lys -30 -25 -20 gca ggc agc gtg ccg tcc ctg gct gca ggg ctg ctc ttt ggc agt cta Ala Gly Ser Val Pro Ser Leu Ala Ala Gly Leu Leu Phe Gly Ser Leu	107
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251 299
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251 299
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251 299
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251 299
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251 299
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251 299 347 395
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251 299
ggggcetteg tgagaceggt geaggeetgg ggtagtetee tgtetggaca gagaagagaa aa atg cag gac act gge tea gta gtg eet ttg cat tgg ttt gge ttt Met Gln Asp Thr Gly Ser Val Val Pro Leu His Trp Phe Gly Phe -45 -40 -35 gge tac gca gca ctg gtt gct tet ggt ggg atc att gca aaa Gly Tyr Ala Ala Leu Val Ala Ser Gly Gly Ile Ile Gly Tyr Val Lys -30 gca gge age gtg ccg tee etg get gea ggg etg ete ttt gge agt eta Ala Gly Ser Val Pro Ser Leu Ala Ala Gly Leu Leu Phe Gly Ser Leu -15 gce gge etg ggt get tac eag etg tet eag gat eea agg aac gtt tgg Ala Gly Leu Gly Ala Tyr Gln Leu Ser Gln Asp Pro Arg Asn Val Trp 1 gtt tte eta get aca tet ggt ace ttg get gge att atg gga atg agg Val Phe Leu Ala Thr Ser Gly Thr Leu Ala Gly Ile Met Gly Met Arg 20 25 10 15 26 27 27 28 29 20 25 30 20 25 30 26 27 28 29 20 25 30 20 25 30 26 27 28 29 20 25 30 20 25 30 26 27 28 29 20 25 30 20 25 30 26 27 28 29 29 20 25 30 20 20 25 30 26 27 28 29 29 20 20 20 20 20 20 20 20	107 155 203 251 299 347 395
ggggccttcg tgagaccggt gcaggcctgg ggtagtctcc tgtctggaca gagaagagaa	107 155 203 251 299 347 395 448 508
ggggcetteg tgagaceggt geaggeetgg ggtagtetee tgtetggaca gagaagagaa aa atg cag gac act ggc tea gta gtg cet ttg cat tgg ttt ggc ttt Met Gln Asp Thr Gly Ser Val Val Pro Leu His Trp Phe Gly Phe -45 -40 -35 ggc tac gca gca ctg gtt gct tet ggt ggg atc att ggc tat gta aaa Gly Tyr Ala Ala Leu Val Ala Ser Gly Gly Ile Ile Gly Tyr Val Lys -30 gca ggc agc gtg ccg tee etg get gca ggg etg ete ttt ggc agt eta Ala Gly Ser Val Pro Ser Leu Ala Ala Gly Leu Leu Phe Gly Ser Leu -15 gce ggc etg ggt get tac eag etg tet eag gat eag aac gtt tgg Ala Gly Leu Gly Ala Tyr Gln Leu Ser Gln Asp Pro Arg Asn Val Trp 1 gtt tee eta get aca tet ggt ace ttg get gge att atg gga atg agg Val Phe Leu Ala Thr Ser Gly Thr Leu Ala Gly Ile Met Gly Met Arg 20 tte tac eac tet gga aaa tee atg eet gea ggt tta att gea ggt gee Phe Tyr His Ser Gly Lys Phe Met Pro Ala Gly Leu Ile Ala Gly Ala 35 agt ttg etg atg gte gee aaa gtt gga gtt agt atg tte aac aga eec Ser Leu Leu Met Val Ala Lys Val Gly Val Ser Met Phe Asn Arg Pro 50 60 cat tageagaagt catgtteeag ettagaetga tgaagaatta aaaatetgea	107 155 203 251 299 347 395 448 508

```
<211> 522
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 2..163
<221> polyA_signal
<222> 488..493
<221> polyA_site
<222> 511..522
<400> 98
c gag att gcg ggc tat ggc gcc gaa ggt ttt tcg tca gta ctg gga tat
                                                                      49
 Glu Ile Ala Gly Tyr Gly Ala Glu Gly Phe Ser Ser Val Leu Gly Tyr
                                      10
                                                         15
ccc cga tgg cac cga ttg cca ccg caa agc cta cag cac cac cag tat
                                                                      97
Pro Arg Trp His Arg Leu Pro Pro Gln Ser Leu Gln His His Gln Tyr
            20
                                25
                                                    30
tgc cag cgt cgc tgg cct gac cgc cgc tgc cta cag agt cac act caa
                                                                     145
Cys Gln Arg Arg Trp Pro Asp Arg Cys Leu Gln Ser His Thr Gln
                            40
       35
                                                                     193
tcc tcc ggg cac ctt cct nntgaaggag tggctaaggt tggacaatac
Ser Ser Gly His Leu Pro
    50
acgttcactg cagctgctgt cggggccgtg tttggcctca ccacctgcat cagcgcccat
                                                                     253
gtccgcgaga agcccgacga ccccctgaac tacttccccg gtggctgcgc cnggaggcct
                                                                     313
gactotggga gcacgcacgc acaactacgg gattggcgcc gccgcctgcg tgtactttgg
                                                                     373
                                                                     433
catagoggcc tccctggtca agatgggccg gctggagggc tgggaggtgt ttgcaaaacc
caaggtgtga gccctgtgcc tgccgggacc tccagcctgc agaatgcgtc cagaaataaa
                                                                     493
                                                                     522
ttctgtgtct gtgtgtgaaa aaaaaaaaa
<210> 99
<211> 956
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 13..465
<221> sig_peptide
<222> 13..75
<223> Von Heijne matrix
      score 3.9
      seq PVAVTAAVAPVLS/IN
ngagteggga aa atg get geg agt aen ten atg gne eeg gtg get gtg aeg
                                                                       51
              Met Ala Ala Ser Thr Ser Met Xaa Pro Val Ala Val Thr
                                       -15
                                                           -10
                  -20
                                                                       99
gcg gca gtg gcg cct gtc ctg tcc ata aac agc gat ttc tca gat ttg
Ala Ala Val Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu
            - 5
                                                                       147
cgg gaa att aaa aag caa ctg ctg ctt att gcg ggc ctt acc cgg gag
Arg Glu Ile Lys Lys Gln Leu Leu Leu Ile Ala Gly Leu Thr Arg Glu
                                             20
                        15
                                                                       195
cgg ggc cta cta cac agt agc aaa tgg tcg gcg gag ttg gct ttc tct
```

WO 99/31236 -75- PCT/IB98/02122

Arg Gly Leu Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser

25	Gry	Deu	neu	1113	30	ser	пуэ	ILD	361	35	GIU	Dea	AIG	PIIC	40	
			-+-	cct		~~~	636	ctg	C 2 2		cct		cct	att		243
				Pro				Leu	Gln					Ile		213
				45					50					55		
								gcc								291
Glu	Glu	Asp	Ala 60	Gln	Asp	Met	Asp	Ala 65	Tyr	Thr	Leu	Ala	Lys 70	Ala	Tyr	
ttt	gac	gtt	aaa	gag	tat	gat	cgg	gca	gca	cat	ttc	ctg	cat	ggc	tgc	339
								Ala								
aat	agc	aaq	aaa	acc	tat	ttt	cta	tat	ato	tat	tcc	aga	tat	ctq	ata	387
	Ser	_		_			_	Tyr	_		Ser	_				
	90					-					100					435
								gcc								433
_	Ala	ile	Leu	гàз		HIS	ser	Ala	Pne		GIU	Thr	Ser	ite		
105					110					115					120	4.5.5
								ttt		tage	ctta	gca	gtgg	gcca	ct	485
Arg	Thr	Asn	Gly	Lys 125	Val	Lys	Ser	Phe	Lys 130							
gaat	gaat	at a	actt	tatad	a ta	agcaa	taa	t aa	aaaa	aaqa	tat	cata	aat .	aaag	ttaaaa	545
															ctgatt	605
															gtgtaa	665
															gtttat	725
															aatgca	785
																845
_					_	-			-						tgaaac	
	_							_	_				-		aaaaaa	905
catt	ttat	gt a	acnt	nncai	tt t	cctag	gtac	a gg	ttga	gtat	ccc	ttat	ttg	a		956
<211 <212 <213 <226 <221 <222 <222 <222 <222 <222 <222)> CI 2> 20 1> 8: 2> 20 3> Vo 8: 1> po 1> po 1> po	OS O	epti 4 eijn 3.9	de e ma LMLG mal												
	0 > 1															F 2
cag	ggtc	ctg	cato	ctac	c at Me -2	t Se	g at r Me	g go	et gt La Va	al G	aa a lu Ti 20	hr P	tt g he G	gc t ly P	tc ttc he Phe -15	52
ato	gca	act	atc	a a a a			ato	q cto	q q q			t ct	g cc	a aa	c agc	100
Met	Ala	Thr	· Val	Gly	Le	Let	Me	t Le	. Gly	y Va	l Th	r Le	u Pr	o As 1	n Ser	
				-10							~	c	~ · · ·		c acc	148
tac Tyr	Trp	cga Arg 5	y Val	s ccc Ser	Thi	r Val	Hi:	s Gl	y Asi	n Va	l Il	e Th	r Th	r As	n Thr	110

atc	ttc	gag	aac	ctc	tgg	ttt	agc	tgt	gcc	acc	gac	tcc	ctg	ggc	gtc	196
								Cys								
	20				-	25					30					
tac	aac	tgc	tgg	gag	ttc	ccg	tcc	atg	ctg	gcc	ctc	tct	ggg	tat	att	244
Tyr	Asn	Суз	Trp	Glu	Phe	Pro	Ser	Met	Leu	Ala	Leu	Ser	Gly	Tyr	Ile	
35					4.0					45					50	
cag	gcc	tgc	cgg	gca	ctc	atg	atc	acc	gcc	atc	ctc	ctg	ggc	ttc	ctc	292
								Thr								
		_	-	55					60					65		
ggc	ctc	ttg	cta	ggc	ata	gcg	ggc	ctg	cgc	tgc	acc	aac	att	999	ggc	340
Gly	Leu	Leu	Leu	Gly	Ile	Ala	Gly	Leu	Arg	Cys	Thr	Asn	Ile	Gly	Gly	
			70					75					80			
ctg	gag	ctc	tcc	agg	aaa	gcc	aag	ctg	gcg	gcc	acc	gca	ggg	gcc	CCC	388
								Leu								
		85			-		90					95				
cac	att	ctg	gcc	ggt	atc	tgc	999	atg	gtg	gcc	atc	tcc	tgg	tac	gcc	436
His	Ile	Leu	Ala	Gly	Ile	Cys	Gly	Met	Val	Ala	Ile	Ser	Trp	Tyr	Ala	
	100					105					110					
ttc	aac	atc	acc	cgg	gac	ttc	ttc	gac	ccc	ttg	tac	CCC	gga	acc	aag	484
Phe	Asn	Ile	Thr	Arg	Asp	Phe	Phe	Asp	Pro	Leu	Tyr	Pro	Gly	Thr	Lys	
115					120					125					130	
tac	gag	ctg	ggc	CCC	gcc	ctc	tac	ctg	999	tgg	agc	gcc	tca	ctg	atc	532
Tyr	Glu	Leu	Gly	Pro	Ala	Leu	Tyr	Leu	Gly	Trp	Ser	Ala	Ser	Leu	Ile	
-				135					140					145		
tcc	atc	ctg	ggt	ggc	ctc	tgc	ctc	tgc	tcc	gcc	tgc	tgc	tgc	ggc	tct	580
Ser	Ile	Leu	Gly	Gly	Leu	Cys	Leu	Сув	Ser	Ala	Cys	Cys	Cys	Gly	Ser	
			150					155					160			
gac	gag	gac	cca	gcc	gcc	agc	gcc	cgg	cgg	CCC	tac	cag	gct	cca	gtg	628
Asp	Glu	Asp	Pro	Ala	Ala	Ser	Ala	Arg	Arg	Pro	Tyr	Gln	Ala	Pro	Val	
		165					170					175				
tcc	gtg	atg	CCC	gtc	gcc	acc	tcg	gac	caa	gaa	ggc	gac	agc	agc	ttt	676
Ser	Val	Met	Pro	Val	Ala	Thr	Ser	Asp	Gln	Glu	Gly	Asp	Ser	Ser	Phe	
	180					185					190					
ggc	aaa	tac	ggc	aga	aac	gcc	tac	gtg	tag	cagc	tct	ggcc	cgtg	9 9		723
Gly	Lys	Tyr	Gly	Arg	Asn	Ala	Tyr	Val								
195					200											
CCC	cgct	gtc 1	ttcc	cact	gc c	ccaa	ggag	a gg	ggac	ctgg	ccg	gggc	cca	ttcc	cctata	783
gtaa	acct	cag 9	gggc	cggc	ca c	gccc	cgct	c cc	gtag	cccc	gcc	ccgg	cca	cggc	cccgtg	843
tcti	tgca	ctc 1	tcat	ggcc	cc t	ccag	gcca	a ga	actg	ctct	tgg	gaag	tcg	cata	tctccc	903
ctc	tgag	gct 9	ggat	ccct	ca t	cttc	tgac	c ct	gggt	tctg	ggc	tgtg	aag	ggga	cggtgt	963
CCC	cgca	cgt 1	ttgt	attg	tg t	ataa	atac	a tt	catt	aata	aat	gcat	att	gtga	ccgtta	1023
aaaa	aaaa	aaa a	aaaa	aaaa												1041

```
<210> 101
<211> 558
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 103..294

<221> sig_peptide
<222> 103..243
```

<223> Von Heijne matrix score 5.9 seq TWLGLLSFQNLHC/FP.

<400> 101 ttcccatggt ttagaagcat aacctgtaat gtaatgcaag tcccctaact ccctggttgc

WO 99/31236 -77- PCT/IB98/02122

taacattaac ttccttaagt aataatcaat gaaagaaatt Ct atg cat ggt ttt Met His Gly Phe -45	114
gaa ata ata tcc ttg aaa gag gaa tca cca tta gga aag gtg agt cag Glu Ile Ile Ser Leu Lys Glu Glu Ser Pro Leu Gly Lys Val Ser Gln	162
-40 -35 -30 ggt cot tig tit aat gig act agi ggo toa toa toa coa gig acc igg	210
Gly Pro Leu Phe Asn Val Thr Ser Gly Ser Ser Pro Val Thr Trp -25 -20 -15	210
ttg ggc cta ctc tcc ttc cag aac ctg cat tgc ttc cca gac ctc ccc	258
Leu Gly Leu Leu Ser Phe Gln Asn Leu His Cys Phe Pro Asp Leu Pro -10 -5 1 5	
act gag atg cct cta aga gcc aaa gga gtc aac act tgagcctagg Thr Glu Met Pro Leu Arg Ala Lys Cly Val Asn Thr 10	304
gtgggctaca acaaaagatt ctaatttacc ttgcttcatc taggtccagg ccccaagtag	364
cttgctgaag gaacttaaaa agtagctgtt atttattgta ttgtataagc taaaaacatt	424
tatttttgtt gaatcgaaac aattccatgt agcaatcttt tttctgttca cggtgtttgt	484 544
gatagaacct taaattccgc aagcatcagt tttttgaaaa aatgggaatt gaccggatag taacaggcaa agtt	558
<210> 102	
<211> 730	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 81518	
<pre><221> sig_peptide <222> 81173 <223> Von Heijne matrix score 3.9 seq ILFHGVFYAGGFA/IV</pre>	
564 121.1601.11 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
<400> 102	60
ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg	113
Met Met Trp Gln Lys .Tyr Ala Gly Ser Arg Arg -30 -25	
tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc	161
Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala	
-20 -15 -10 -5 ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg	209
Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg	
1 5 10	257
get tta tat tae aag ttg gea gtg gag cag etg cag age cat eee gag	257
Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu 15 20 25	305
gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu	,,,,
WIR GIU GIU WIN DEU GIY FIO FIO DEU MAN IIE WIN 11 DEU -10	
30 35 40 atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att	353
30 35 40 atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile	353
30 35 40 atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60	353 401
30 35 40 atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60 cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc	
30 35 40 atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60	

WO 99/31236 -78- PCT/IB98/02122

Arg Gly Gly Pro Phe Gln Arg Trp His Leu Asp Glu Val Phe Leu Glu 80 85 90	
ctc aag gat ggt cag cag att cct gtg ttc aag ctc agt ggg gaa aac	497
Leu Lys Asp Gly Gln Gln Ile Pro Val Phe Lys Leu Ser Gly Glu Asn 95 100 105	
ggt gat gaa gtg aaa aag gag tagagacgac ccagaagacc cagcttgctt	548
Gly Asp Glu Val Lys Lys Glu 110 115	
ctagtccatc cttccctcat ctctaccata tggccactgg ggtggtggcc catctcagtg	608
acagacacto otgoaaccoa gttttocago caccagtggg atgatggtat gtgccagcac	668
atggtaattt tggtgtaatt ctaacttggg cacaacgaat gctatttgtc atttttaaac	728
tg	730
<210> 103	
<211> 1098	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 66326	
<221> polyA_signal	
<222> 10661071	
<221> polyA_site	
<222> 10871098	
.400- 103	
<400> 103 ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc	60
Cleberta aldadada craaccedor consumpto organismo and	
chara and the get org are get cat che cea cea age cat get tec	110
ctete atq gag ttg get eeg aca gee egt etg eea eea gge eat ggt tee	
ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser	
ctete atg gag ttg get ceg aca gee egt etg cea eea gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15	
ctete atg gag ttg get ceg aca gec egt etg cea eea gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg eec eat ggt gte etg gga eec aga gea aca gga tet gte ace eac	110
ctete atg gag ttg get ceg aca gee egt etg cea eea gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15	110
ctete atg gag ttg get ceg aca gee egt etg cea eea gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg cee cat ggt gte etg gga eee aga gea aca gga tet gte ace eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30	110
ctete atg gag ttg get ceg aca gee egt etg cea eca gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ecc eat ggt gte etg gga ecc aga gea aca gga tet gte acc eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete ecc eag ate aag eaa egt gee tea gag get ttg ecc	110
tete atg gag ttg get ceg aca gec egt etg cea eca gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ecc eat ggt gte etg gga ecc aga gea aca gga tet gte acc eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete ecc eag ate aag eaa egt gee tea gag get ttg ecc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45	110 158 206
ctete atg gag ttg get ceg aca gec egt etg cea eea gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg eec eat ggt gte etg gga eec aga gea aca gga tet gte ace eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete eec eag ate aag eaa egt gee tea gag get ttg eec Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ett egt eet gte ace eec ate ace aat ttt gag gge age eag	110
ctete atg gag ttg get ceg aca gec egt etg cea eea gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg eec eat ggt gte etg gga eec aga gea aca gga tet gte ace eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete eec eag ate aag eaa egt gee tea gag get ttg eec Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ett egt eet gte ace eec ate ace aat ttt gag gge age eag	110 158 206
ctete atg gag ttg get ceg aca gec egt etg cea eca gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ecc eat ggt gte etg gga ecc aga gea aca gga tet gte ace eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete ecc eag ate aag eaa egt gee tea gag get ttg ecc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ett egt eet gte ace eec ate ace aat ttt gag gge age eag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60	110 158 206 254
ctete atg gag ttg get ceg aca gec egt etg cea eca gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ecc eat ggt gte etg gga ecc aga gea aca gga tet gte acc eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete ecc eag ate aag eaa egt gee tea gag get ttg ecc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ett egt eet gte acc ecc ate ace aat ttt gag gge age eag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60 tet eag gae eac agt gga ate ttt gge etg gta aca aac etg gaa gag	110 158 206
tette atg gag ttg get ceg aca gec egt etg cea eea gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg eec eat ggt gte etg gga eec aga gea aca gga tet gte ace eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete eec eag ate aag eaa egt gee tea gag get ttg eec Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ett egt eet gte ace eec ate ace aat ttt gag gge age eag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60 tet eag gae eac agt gga ate ttt gge etg gta aca aac etg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu	110 158 206 254
ctete atg gag ttg get ceg aca gec egt etg cea eca gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ecc eat ggt gte etg gga ecc aga gea aca gga tet gte ace eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete ecc eag ate aag eaa egt gee tea gag get ttg ecc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ett egt eet gte ace eec ate ace aat ttt gag gge age eag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60 tet eag gae eac agt gga ate ttt gge etg gta aca aac etg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu 65 70 75	110 158 206 254 302
tette atg gag ttg get ceg aca gec egt etg cea eca gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ecc eat ggt gte etg gga ecc aga gea aca gga tet gte ace eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete ecc eag ate aag eaa egt gee tea gag get ttg ecc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ett egt eet gte ace ecc ate ace aat ttt gag gge age eag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60 tet eag gae eac agt gga ate ttt gge etg gta aca aac etg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu 65 70 75 etg gag gtg gae gat tgg gag tte tggageetetg eaaactgtge geatteteea	110 158 206 254
ctete atg gag ttg get ceg aca gec egt etg cea eca gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ecc eat ggt gte etg gga ecc aga gea aca gga tet gte ace eac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete ecc eag ate aag eaa egt gee tea gag get ttg ecc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ett egt eet gte ace eec ate ace aat ttt gag gge age eag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60 tet eag gae eac agt gga ate ttt gge etg gta aca aac etg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu 65 70 75	110 158 206 254 302
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60 tct cag gac cac agt gga atc ttt ggc ctg gta aca aac ctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu 65 70 75 ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctcca Leu Glu Val Asp Asp Trp Glu Phe 80	110 158 206 254 302 356
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60 tct cag gac cac agt gga atc ttt ggc ctg gta aca aac ctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu 65 70 75 ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctcca Leu Glu Val Asp Asp Trp Glu Phe 80 85	110 158 206 254 302 356 416
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60 tct cag gac cac agt gga atc ttt ggc ctg gta aca aac ctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu 65 70 75 ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctcca Leu Glu Val Asp Asp Trp Glu Phe 80 85 gccagggatg cagaggccac ccagaggccc ttcctgaggg ccggccacat tcccgccctc ctgggcagat tgggtagaaa ggacattctt ccaggaaagt tgactgctgg ctgattggga	110 158 206 254 302 356 416 476
ctete atg gag ttg get ceg aca gec egt etg eca eca gge eat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ece eat ggt gte etg gga ece aga gea aca gga tet gte ace eae Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 etc tet ett ete eee eag ate aag eaa egt gee tea gag get ttg ece Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ett egt eet gte ace eee ate ace aat ttt gag gge age eag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 5 60 tet eag gae eae agt gga ate ttt gge etg gta aca aac etg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu 65 70 75 etg gag gtg gae gat tgg gag tte tgageetetg eaaaetgtge geatteteea Leu Glu Val Asp Asp Trp Glu Phe 80 85 geeagggatg eagaggeeae eeagaggeee tteetgagag eeggeeaeat teeegeete etgggeagat tgggtagaaa ggacattett eeaggaaagt tgaetgetgg etgattgga aagaaaatee tgggtagaaa ggacattett eeaaggettt tgagacacaa gggaatetea	110 158 206 254 302 356 416 476 536
Ctete atg gag ttg get ceg aca gec egt etg cea eca gge cat ggt tee Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1	110 158 206 254 302 356 416 476 536 596
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 ctc cag gac cac agt gga atc ttt ggc ctg gta aca aac ctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu 65 70 75 ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctca Leu Glu Val Asp Asp Trp Glu Phe 80 85 gccagggatg cagaggccac ccagaggccc ttcctgagg ccggccacat tcccgccctc ctgggcagat tgggtagaaa ggacattctt ccaggaaagt tgactgctgg ctgattgga aagaaaatcc tgggaagata cttcactgct ccaaggcttt tgagacacaa gggaatctca acaaccaggg atcagaggg tccaaagccg acattcccag tcctgtagc tcaggtgacc tcctccgcac aagaggagt ctgctctgc cctgggagct gaattccaag cccagggttt	110 158 206 254 302 356 416 476 536 596 656
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 25 30 ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 55 60 tct cag gac cac agt gga atc ttt ggc ctg gta aca aac ctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu 65 70 75 ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattetcca Leu Glu Val Asp Asp Trp Glu Phe 80 85 gccagggatg cagaaggccac ccagaggcc ttcctgaggg ccggccacat tcccgccctc ctgggcagat tgggtagaaa ggacattett ccaggaaagt tgactgctgg ctgattgga aagaaaatcc tgggagaata cttcactgct ccaaaggctt tgagacacaa gggaatctca acaaccaggg atcaggagat ctgccttggc cctggagct gaattccaag ccctcctcagaggact ctcctcagagg ccggccacat tcccggccttc ctctccgcag aagagagat ctccaaagccg acattcccag tcctgtgagc tcaggtgacc ccctcctccagagagaccac cccagaggcc tccctggagct gaattccaag cccagggttt ccctcccgcag aagagagatg ctgctctggc cctggagct tgcgaccagc ctcattctac	110 158 206 254 302 356 416 476 536 596 656 716
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga cca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 20 25 30 ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ctt cgt cct gtc acc ccc atc acc act ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 55 60 tct cag gac cac agt gga atc ttt ggc ctg gta aca cctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu Glu 65 70 75 ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctcca Leu Glu Val Asp Asp Trp Glu Phe 80 85 gccagggatg cagaggccac ccagaggccc ttcctgaggg ccggccacat tcccgcctc ctggggcagat tgggtagaaa ggacattctt ccaggaaagt tgactgctgg acaacacaggga acaacacaggg atcaaaggagg cccaaagccg cccaaggctt tgacgacaaa gggaatctca acaaccaggg atcaagaagt ctccaaagccg acattccca tcctcggacaga tccaaagagg ccgccctct tcccaggact tgacgacaa gggaatctca acaaccaggg atcaagaaga cgccactct tcccaggact tgacgaccaa cccagggtt tgacgaccaa cccagggtt tgacgaccaa cccagggtt tgacgcccaa cccagggtt tgacgaccaa cccagggtt tgacgcccaac cccagggtt tgacgcccaac tcctccaggtact tgccccaaa cccagggtt tgacgcccaac cccagggtt tgacgcccaac cccagggtt tgacgcccaacac cccagggtt tgacgcccaac tcccagggtt tgacccctaa cccagggtt tgcccccaacctctt tcccagtgct tgacaccaa gggaacctca tccccagggtt tgacccctaa cccagggtt tgcccccaacctct tcccaggacc tcctccaacacccag cccagggtt tgccaacctct tcccaggacc tccattctac tccaaccttt tcccagtgct tgcaacacac cccagggtt tgccccctaa cccagaggcc ctcattctac tccaaccttct tcccagtgct tgcaacacac cccagggtt tccaaccttct tcccagtgct tgcaacacac cccagggtt	110 158 206 254 302 356 416 476 536 596 656 716 776
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga cca aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 20 25 30 ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 55 60 tct cag gac cac agt gga atc ttt ggc ctg gta aca cctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu Glu 65 70 75 ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctcca Leu Glu Val Asp Asp Trp Glu Phe 80 85 gccagggatg cagaagccac ccagaagccc ttcctgagg ccggccacat tcccgcctc ctgggcagat tgggtagaaa ggacattctt ccaagaagt tgagcacaa gggaatctca acaaccaggg atcagaagt ctgcctcgc ccaaagcgt ttggagaacca gggaatctca acaaccaggg atcagaaga ctgccctctc tccaagaagct ttggagaacaa ggaatctca acaaccaggg atcagaaga ctgccctct tccaagaagct tggagaacca cccagaggcc tccccgcaga aagaagaatg ctgccctcgc cctagatgct tggagaacaa ggaatctca acaaccagga acaagaagaac ctccaaagccg ccctggagact tggagaacaa ctccaagacct tcccagaggacc tccccaagagct tggagaacaa ggaatctca acaaccagga acaagaagaac ctccaaagccg ccctggagacc tcccaagacct tcccagaggcc ctcaatctca acaaccagga tcccaaagacga cccaacctct tcccagagacct tggagaacaag ttggacacaa ggaatctcaactcaa	110 158 206 254 302 356 416 476 536 596 656 716 776 836
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 20 25 30 ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 60 tct cag gac cac agt gga atc ttt ggc ctg gta aca aac ctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu Glu 65 70 75 ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctca Leu Glu Val Asp Asp Trp Glu Phe 80 85 gccagggatg caggaggcac ccagaggccc ttcctgaggg ccggccacat tcccggcagat tgggtagaaa ggacattctt ccaggaaagt tgactgctgg tcgatagaa agaaaatcc tgggaagat ctcacagcc ccaaggctt tgagacacaa gggaatctca acaaccaggg atcaggagat ctcacagccg acattccca tccccgcag aagagagat ctccaagagc cccaggagct tcccagaggct gaattccaa cccagggttt ggctcctaa acccagggac ctccccagagac tccccagagac tcccagagac tccccagagac tcccagagac gaatcccaa gacaacac tccccagagac tccccagagac tcccagagac tcccagagac gaaagagac ttcctccctcc cccagagac cccagagac cccagagac cccagagac cccagagac cccagagac gaaaagac gaaaagac gaaaagac ctcccagagac cccagagac ccccagagac cccagagac cccagagac ccccagagac cccagagac ccccagagac cccagagac cccagaagac	110 158 206 254 302 356 416 476 536 596 656 716 776 836 896
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1	110 158 206 254 302 356 416 476 536 596 656 716 776 836 896 956
Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser 1 5 10 15 ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His 20 20 25 30 ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro 35 40 45 gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln 50 60 tct cag gac cac agt gga atc ttt ggc ctg gta aca aac ctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu Glu 65 70 75 ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctca Leu Glu Val Asp Asp Trp Glu Phe 80 85 gccagggatg caggaggcac ccagaggccc ttcctgaggg ccggccacat tcccggcagat tgggtagaaa ggacattctt ccaggaaagt tgactgctgg tcgatagaa agaaaatcc tgggaagat ctcacagcc ccaaggctt tgagacacaa gggaatctca acaaccaggg atcaggagat ctcacagccg acattccca tccccgcag aagagagat ctccaagagc cccaggagct tcccagaggct gaattccaa cccagggttt ggctcctaa acccagggac ctccccagagac tccccagagac tcccagagac tccccagagac tcccagagac gaatcccaa gacaacac tccccagagac tccccagagac tcccagagac tcccagagac gaaagagac ttcctccctcc cccagagac cccagagac cccagagac cccagagac cccagagac cccagagac gaaaagac gaaaagac gaaaagac ctcccagagac cccagagac ccccagagac cccagagac cccagagac ccccagagac cccagagac ccccagagac cccagagac cccagaagac	110 158 206 254 302 356 416 476 536 596 656 716 776 836 896

tcagagacgc aaaaaaaaa aa	1098
<210> 104	
<211> 346	
<212> DNA	
<213> Homo sapiens	
<220>.	
<221> CDS	
<222> 170289	
<221> sig_peptide	
<222> 170250 <223> Von Heijne matrix	
score 3.6	
seg LTLLLITPSPSPL/LF	
acq athuntrorors, a.	
<400> 104 ccatttgage eccaecaegg aggttatgtg gteccaaaag gaatgatgge caagcaatta	60
attiticate ctagetetta gettgettet geattgattg getttacaca actggeattt	120
agtotgoatt acacaaatag acactaattt atttggaaca agcagcaaa atg aga act	178
Met Arg Thr	
tta ttt ggt gca gtc agg gct cca ttt agt tcc ctc act ctg ctt cta	226
Leu Phe Gly Ala Val Arg Ala Pro Phe Ser Ser Leu Thr Leu Leu Leu	
-20 -15 -10	
ate ace cet tet eee age eet ett eta tit gat aga ggt etg tee ete	274
Ile Thr Pro Ser Pro Ser Pro Leu Leu Phe Asp Arg Gly Leu Ser Leu	
-5 1 5 aga toa goa atg tot tagecoctot cotetettee atteetteet gttggtacte	329
Arg Ser Ala Met Ser	
atttcttcta actttta	346
	-
<210> 105	
<211> 685	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 36497	
<221> polyA_signal	
<222> 650655	
<221> polyA site	
<222> 663685	
<400> 105	53
aagttetgeg etggteggeg gagtageaag tggee atg ggg age ete age ggt Met Gly Ser Leu Ser Gly	23
1 5	101
ctg cgc ctg gca gca gga agc tgt ttt agg tta tgt gaa aga gat gtt	101
Leu Arg Leu Ala Ala Gly Ser Cys Phe Arg Leu Cys Glu Arg Asp Val	
tcc tca tct cta agg ctt acc aga agc tct gat ttg aag aga ata aat	149
Ser Ser Ser Leu Arg Leu Thr Arg Ser Ser Asp Leu Lys Arg Ile Asn	

25 30 35 qqa ttt tgc aca aaa cca cag gaa agt ccc gga gct cca tcc cgc act	197											
Gly Phe Cys Thr Lys Pro Gln Glu Ser Pro Gly Ala Pro Ser Arg Thr												
40 45 50												
tac aac aga gtg cct tta cac aaa cct acg gat tgg cag aaa aag atc	245											
Tyr Asn Arg Val Pro Leu His Lys Pro Thr Asp Trp Gln Lys Lys Ile												
55 60 65 70												
ctc ata tgg tca ggt cgc ttc aaa aag gaa gat gaa atc cca gag act	293											
Leu Ile Trp Ser Gly Arg Phe Lys Lys Glu Asp Glu Ile Pro Glu Thr												
75 80 85												
gto tog ttg gag atg ott gat got goa aag aac aag atg oga gtg aag	341											
Val Ser Leu Glu Met Leu Asp Ala Ala Lys Asn Lys Met Arg Val Lys												
90 95 100												
age age tat eta atg att gee etg acg gtg gta gga tge ate tte atg	389											
Ser Ser Tyr Leu Met Ile Ala Leu Thr Val Val Gly Cys Ile Phe Met												
105 110 115												
gtt att gag ggc aag aag gct gcc caa aga cac gag act tta aca agc	437											
Val Ile Glu Gly Lys Lys Ala Ala Gln Arg His Glu Thr Leu Thr Ser												
120 125 130												
ttg aac tta gaa aag aaa gct cgt ctg aaa gag gaa gca gct atg aag	485											
Leu Asn Leu Glu Lys Lys Ala Arg Leu Lys Glu Glu Ala Ala Met Lys												
135 140 145 150												
gcc aaa aca gag tagcagaggt atccgtgttg gctggatttt gaaaatccag	537											
Ala Lys Thr Glu												
gaattatgtt ataacgtgcc tgtattaaaa aggatgtggt atgaggatcc atttcataaa	597											
gtatgatttg cccaaacctg taccatttcc gtatttctgc cgtagaagta gaaataaatt	657											
ttcttaaaaa aaaaaaaaaa aaaaaaaaa	685											
•												
<210> 106												
<211> 554												
<211> 554 <212> DNA												
<211> 554												
<211> 554 <212> DNA <213> Homo sapiens												
<211> 554 <212> DNA <213> Homo sapiens												
<211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS												
<211> 554 <212> DNA <213> Homo sapiens												
<211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320												
<211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal												
<211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320												
<211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544												
<211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site												
<211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544												
<211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site												
<pre><211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106</pre>	50											
<pre><211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccqtcqtq qqqaaqq atq gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</pre>	50											
<pre><211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt Met Val Cys Glu Lys Cys Glu Lys Lys Leu Gly</pre>	50											
<pre><211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt Met Val Cys Glu Lys Cys Glu Lys Leu Gly 1</pre> 10												
<pre><211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</pre>	50 98											
<pre><211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</pre>												
<pre><211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</pre>	98											
<pre><211> 554 <212> DNA <213> Homo sapiens </pre> <pre><220> <221> CDS <222> 18320 </pre> <pre><221> polyA_signal <222> 539544 </pre> <pre><221> polyA_site <222> 542554</pre> <pre><400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</pre>												
<pre><211> 554 <212> DNA <213> Homo sapiens </pre> <pre><220> <221> CDS <222> 18320 </pre> <pre><221> polyA_signal <222> 539544 </pre> <pre><221> polyA_site <222> 542554</pre> <pre><400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</pre>	98											
<pre><211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</pre>	98											
<pre><211> 554 <212> DNA <213> Homo sapiens </pre> <pre><220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</pre>	98											
<pre><211> 554 <212> DNA <213> Homo sapiens </pre> <pre><220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</pre>	98											
<pre><211> 554 <212> DNA <213> Homo sapiens </pre> <pre> <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 </pre> <pre> <221> polyA_site <222> 542554 </pre> <pre> <a 10.10"="" doi.org="" href="https:</td><td>98</td></tr><tr><td><pre><211> 554 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 <221> polyA_site <222> 542554 <400> 106 aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt</td><td>98</td></tr><tr><td><pre><211> 554 <212> DNA <213> Homo sapiens </pre> <pre> <220> <221> CDS <222> 18320 <221> polyA_signal <222> 539544 </pre> <pre> <221> polyA_site <222> 542554 </pre> <pre> </pre>												

70 .

290

65

tgt gcc tac aaa aaa ggc atc tgt gcg atg tgt ggn aaa aaa gtt ttg

WO 99/31236 -81- PCT/IB98/02122

Cys Ala Tyr Lys Lys Gly Ile Cys Ala Met Cys Gly Lys Lys Val Leu 80 85 90	
gat acc aaa aac tac aag caa aca tot gto tagatgtatt gatggaattt	340
Asp Thr Lys Asn Tyr Lys Gln Thr Ser Val	
95 100 ctggctttct aaatgatttt actttctgcc ttgaattttc aaggcataga tgtcaactta	400
cagaataaca tgttttaaga taattaagtt taaaccagag aatttgattg ttactcattt	460
tgctctcatg ttctaaacag caacagtgta actagtcttt tgttgtaaat ggttattttc	520
cttataagaa ttttaagaac taaaaaaaaa aaaa	554
<210> 107	
<211> 1678	
<212> DNA <213> Homo sapiens	
<220>	
<221> CDS	
<222> 71. 1438	
<221> sig_peptide	
<222> 71136	
<223> Von Heijne matrix	
score 3.5 seq AAPVAAGLGPVIS/RP	
<221> polyA_signal	
<222> 16441649	
<221> polyA_site	
<222> 16651678	
<400> 107	60
<400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgccct cccgacctt atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta	60 109
<400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgccct cccgaccctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta Met Phe Glu Glu Pro Glu Trp Ala Glu Ala Ala Pro Val	
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgccct cccgaccctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgccct cccgaccctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgccct cccgaccctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253 301
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253 301 349
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgcctt cccgaccetc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253 301
<pre> <400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accetgcctt cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253 301 349 397
<pre> <400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgccct cccgacctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253 301 349
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgcctc cccgaccctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253 301 349 397
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaaagagcgg ggactcggcg accctgcct cccgaccctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253 301 349 397
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaagagcgg ggactcggcg accctgcctcccgaccctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta Met Phe Glu Glu Pro Glu Trp Ala Glu Ala Ala Pro Val</pre>	109 157 205 253 301 349 397 445
<pre><400> 107 ccgacttcca gaggagcgct gtgcacgtgg agaaagagcgg ggactcggcg accctgcct cccgaccctc atg ttc gaa gag cct gag tgg gcc gag gcg gcc cca gta</pre>	109 157 205 253 301 349 397 445

WO 99/31236 -82- PCT/IB98/02122

			-	_	cac	_	-		_	_						541
11e	Asn	Ser	Ala	Gin	His	Leu	Asp	Asn	Val	Asp 130	Gin	rnr	Gly	Pro	Lуs 135	
acc	taa	aag	aat	agt	act	aca	aat	qat	cca	cca	aaq	caa	agc	cct	ggg	589
					Thr											
tcc	act	tcc	cct		ccc	cct	cat	aca		age	cac	aad	cad	taa	caa	637
			Pro		Pro			Thr					Gln			
			155				202	160	224	226	225		165		aat	685
					aag											003
		170			Lys		175					180				
					gcc											733
	185		_		Ala	190					195					
gtg	tct	cct	gtt	ccc	agg	aca	gac	agc	cat	999	gct	cgg	gca	999	gct	781
Val	Ser	Pro	Val	Pro	Arg	Thr	Asp	Ser	His	Gly	Ala	Arg	Ala	Gly	Ala	
200					205					210					215	
ttg	cga	gcc	cgc	atg	gca	cag	cgg	ctg	gat	999	gcc	cga	ttt	cgc	tac	829
Leu	Arg	Ala	Arg	Met	Ala	Gln	Arg	Leu	Asp	Gly	Ala	Arg	Phe	Arg	Tyr	
	. –		_	220					225					230		
ctc	aat	gaa	cag	ttg	tac	tca	ggg	CCC	agc	agt	gct	gca	cag	cgt	ctc	877
Leu	Asn	Ğlu	Gln 235	Leu	Tyr	Ser	Gly	Pro 240	Ser	Ser	Ala	Ala	Gln 245	Arg	Leu	
ttc	caq	gaa		cct	gag	act	ttt	ctt	ctc	tac	cac	cgc	ggc	ttc	cag	925
Phe	Gln	Glu	Asp	Pro	Glu	Ala	Phe	Leu	Leu	Tyr	His	Arq	Gly	Phe	Gln	
	•	250					255			- 2 -		260				
age	caa		aaσ	aag	tgg	cca		cag	cca	ata	gac		atc	acc	agg	973
Ser	Gln	Val	Lva	Lve	Trp	Pro	Leu	Gln	Pro	Val	Asp	Ara	Ile	Ala	Arg	
261	265	V G A	my s	my a	11p	270	204	٠			275	• 5				
cat		cac	cad	caa	cct		tec	cta	ata	ata		дас	ttc	aac	tat	1021
Aen	LAU	Ara	Gla	722	Pro	Δla	Ser	Leu	Val	Val	Ala	Asp	Phe	Glv	Cvs	
280	Deu	~-3	0111	~~9	285	71.44				290				1	295	
	~ · ·	+ ~ ~			gct	+ = =	agt	arc	caa		cct	ata	cat	tac		1069
299	yac Nan	Cvo	720	Ley	Ala	Cor	Cor	Tle	723	Agn	Pro	Val	His	Cvs	Phe	
GIY	waħ	Cys	Arg	300	AIG	261	361	110	305	70				310		
~~~	++~	~~ <b>+</b>			gac	cct	200	atc		ata	tat	gac	atσ		cag	1117
yac	Lay	712	507	Len	Asp	Dro	470	Val	Thr	Val	Cvs	Agn	Met	Ala	Gln	
ASP	Leu	Ala	315	пеп	vaħ	PIO	ALG	320	****	V 44.1	Cyo	ASP	325			
a++	cct	++~		~at	gag	tet	ata		ata	act	ata	ttt		ctt	tca	1165
Val	Dro	Lev	Glu	yar	Glu	Sar	Val	Asn	Val	Ala	Val	Phe	CVB	Leu	Ser	
val	PiU	330	GIU	voħ	Giu	361	335	vaħ				340	-,-			
cta	atσ		acc	aac	atc	agg		ttc	cta	gag	gag		aat	aga	qta	1213
Leu	Met	Glv	Thr	Acn	Ile	Ara	Asp	Phe	Leu	Glu	Glu	Ala	Asn	Ara	Val	
200	345	017	****			350					355			_		
cta		cca	aaa	aat	ctc		aaa	ata	act	дад		age	agc	cac	ttt	1261
Len	Lve	Dro	222	Glv	Leu	T.eu	Lvs	Val	Ala	Glu	Val	Ser	Ser	Arq	Phe	
360	Lys	FIO	GI	O17	365		2,0			370				ر	375	
	a . +	~++		200		cta	caa	act	ata		аад	CEA	gac	ttc	aag	1309
gag	gat	yet val	va-	The	Phe	TAN	723	Ala	V=1	Thr	Lve	Leu	Glv	Phe	Lvs	
GIU	Asp	vai	Arg			Den	Arg	AIG	385	1112	<b>-</b> 173	204	017	390	, _	
				380				300		-+-		++0				1357
att	gtc	CCC	aag	gac	ctg	acc	200	age	uio	200	Dhe	Ten	Dhe	Acr	ttc Dhe	
ııe	Val	ser		Asp	Leu	Thr	ASI		.115	PHE	Pile	peu	405	ns.	Phe	
			395					400								1405
caa	aag	act	333	CCC	cct	ctg	gta	999	CCC	aag	905	cag	Tal	- CC	ggc	1403
Gln	Lys		Gly	Pro	Pro	Leu		GIY	PID	Lys	Ala			sei	Gly	
		410					415					420				1450
ctg	cag	ctt	cag	cca	tgt	ctc	tac	aag	cgc	agg	tga	cctc	rgg	atct	tccttg	1458
Leu		Leu	Gln	Pro	Cys			Lys	Arg	Arg						
	425					430								_		
aga	9999	agg	caga	tctc	aa a	ctcc	aggc	t ca	gaac	tgtg	aag	actg	itt	ccgg	gcctggc	1518
tgt	gage	caa	gacc	tggt	tc c	tggt	ggac	c ct	gagg	асаз	agt	gtga	taa	aaco	ctctggc	1578

1638 1678

tragacttgc totactgaag gottottggt tataagatgc ataaagtcac tggggctagc

<210> 108 <211> 494 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 25..318 <221> sig_peptide <222> 25..75 <223> Von Heijne matrix score 7.4 seg FFLLLQFFLRIDG/VL <221> polyA signal <222> 452..457 <221> polyA_site <222> 482..494 <400> 108 aggotgagtg tgaagattag agta atg cot tot ago tit tic oig oig tig 51 Met Pro Ser Ser Phe Phe Leu Leu Leu -15 99 cag ttt ttc ttg aga att gat ggg gtg ctt atc aga atg aat gac acg Gln Phe Phe Leu Arg Ile Asp Gly Val Leu Ile Arg Met Asn Asp Thr -5 1 aga ctt tac cat gag gct gac aag acc tac atg tta cga gaa tat acg 147 · Arg Leu Tyr His Glu Ala Asp Lys Thr Tyr Met Leu Arg Glu Tyr Thr 15 20 tca cga gaa agc aaa att tct agt ttg atg cat gtt cca cct tcc ctc 195 Ser Arg Glu Ser Lys Ile Ser Ser Leu Met His Val Pro Pro Ser Leu 35 25 30 ttc acg gaa cct aat gaa ata tcc cag tat tta cca ata aag gaa gca 243 Phe Thr Glu Pro Asn Glu Ile Ser Gln Tyr Leu Pro Ile Lys Glu Ala 50 45 291 gtt tgt gag aag cta ata ttt cca gaa aga att gat cct aac cca gca Val Cys Glu Lys Leu Ile Phe Pro Glu Arg Ile Asp Pro Asn Pro Ala 65 60 338 gac tca caa aaa agt aca caa gtg gaa taaaatgtga tacaacatat Asp Ser Gln Lys Ser Thr Gln Val Glu 80 actcactatg gaatctgact ggacaccttg gctatttgta aggggttatt tttattatga 398 458 gaattaattg ccttgtttat gtacagattt tctgtagcct taaaggaaaa aaaaataaag 494 atogttacag gcaggtttca ctcaaaaaaa aaaaac

<210> 109 <211> 714 <212> DNA <213> Homo sapiens <220> <221> CDS

<222> 84..332

```
<221> sig_peptide
<222> 84..170
<223> Von Heijne matrix
      score 5.2
      seq PCYYLGLFQRALA/SV
<221> polyA_site
<222> 702..714
<400> 109
                                                                   60
cctatctctt ctgctggctg ggctcaatgc cgcgggtgag cgttcggccg aggctgctcc
taccettgag tgatgtgeet tga atg acg etg ett tea tte get get tte acg
                        Met Thr Leu Leu Ser Phe Ala Ala Phe Thr
                                        -25
                                                                  161
get get the tee gte etc ecc tgt tae tae ett ggg etg ttt eag egg
Ala Ala Phe Ser Val Leu Pro Cys Tyr Tyr Leu Gly Leu Phe Gln Arg
                                  -10
               -15
                                                                  209
geg etc geg teg gte tte gae cea ett tge gtt tgt tea egt gtg etc
Ala Leu Ala Ser Val Phe Asp Pro Leu Cys Val Cys Ser Arg Val Leu
                          5
                                                                  257
ccg aca cct gta tgt acc ttg gtc gca aca caa gcc gaa aaa ata tta
Pro Thr Pro Val Cys Thr Leu Val Ala Thr Gln Ala Glu Lys Ile Leu
                       20
   15
                                                                  305
gag aat ggg ccc tgt cca acc aag gag gcg gcc cag ctt gtc ggg aag
Glu Asn Gly Pro Cys Pro Thr Lys Glu Ala Ala Gln Leu Val Gly Lys
                                      40
                                                          45
                   35
ggc agc gtt tcc gcc aga aat gct tcg tgaaaggcac ttgagggacc
                                                                  352
Gly Ser Val Ser Ala Arg Asn Ala Ser
               50
ttagcagcat cctcaacagg ccttgtaggg aatgccagaa gaagcagtcc ttggccgggc
                                                                  412
                                                                  472
qqqqtqqctc atqcctqtqq tcccaqcact ttqqqaqqcc qqqqcqqqcq qatcacctqa
                                                                  532
ggtcgggagg tccagaccag cctgaccgac atggagaaac cccgtctnta ctagaaatac
                                                                  592
aaaactagec gggtgtggtg gcgcatgcct gtagtcccag ctactcggga gggtgaggca
                                                                  652
ggagacgttc ttgaacccgg gaggcggagt ttgtggtgag ccgagatcgc gccattgcac
712
                                                                  714
```

<210> 110

<211> 805

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 32..718

<221> sig_peptide

<222> 32..100

<223> Von Heijne matrix
 score 7.4
 seq VLLLAALPPVLLP/GA

<221> polyA_signal

<222> 770..775

<221> polyA_site

<222> 793..805

<400> 110

cctctttcag cccgggatcg ccccagcagg g atg ggc gac aag atc tgg ctg  Met Gly Asp Lys Ile Trp Leu -20													52			
						ctg Leu -10					ccg	gtg				100
						cct Pro										148
ctt Leu	ccc Pro	gcc Ala	ggc Gly 20	cag Gln	aag Lys	gag Glu	tgc Cys	ttc Phe 25	tac Tyr	cag Gln	ccc Pro	atg Met	ccc Pro 30	ctg Leu	aag Lys	196
			gag			tac Tyr		gtt								244
		ttc				tct Ser	cca									292
caa Gln 65	aga	aaa Lys	tca Ser	gat Asp	gga Gly 70	gtt Val	cac His	act Thr	gta Val	gag Glu 75	act	gaa Glu	gtt Val	ggt Gly	gat Asp 80	340
tac	atg Met	ttc Phe	tgc Cys	ttt Phe 85	gac	aat Asn	aca Thr	ttc Phe	agc Ser 90	acc	att Ile	tct Ser	gag Glu	aag Lys 95	gtg Val	388
att Ile	ttc Phe	ttt Phe	gaa Glu 100	tta	atc Ile	ctg Leu	gat Asp	aat Asn 105	atg	gga Gly	gaa Glu	cag Gln	gca Ala 110	caa	gaa Glu	436
caa Gln	gaa Glu	gat Asp 115	tgg	aag Lys	aaa Lys	tat Tyr	att Ile 120	act	ggc Gly	aca Thr	gat Asp	ata Ile 125	ttg	gat Asp	atg Met	484
aaa Lys	ctg Leu 130	gaa	gac Asp	atc Ile	ctg Leu	gaa Glu 135	tcc	atc Ile	agc Ser	agc Ser	atc Ile 140	aag	tcc Ser	aga Arg	cta Leu	532
agc Ser 145	aaa	agt Ser	Gly 999	cac His	ata Ile 150	caa Gln	att Ile	ctg Leu	ctt L <b>eu</b>	aga Arg 155	gca	ttt Phe	gaa Glu	gct Ala	cgt Arg 160	580
gat	cga Arg	aac Asn	ata Ile	caa Gln 165	gaa	agc Ser	aac Asn	ttt Phe	gat Asp 170	aga	gtc Val	aat Asn	ttc Phe	tgg Trp 175	tct Ser	628
atg Met	gtt Val	aat Asn	tta Leu 180	gtg	gtc Val	atg Met	gtg Val	gtg Val 185	gtg	tca Ser	gcc	att	caa Gln 190	Val	tat Tyr	676
atg Met	ctg Leu	Lys	agt	ctg Leu	ttt Phe	gaa Glu	Asp	aag Lys	agg Arg	aaa Lys	agt Ser	aga Arg 205	act Thr			718
						gtaa aaaa			aaat	gagg	cat			caat	aaactg	778 805

<210> 111

<211> 787

<212> DNA

<213> Homo sapiens

<220>

<221> CDS <222> 26..481

<221> sig_peptide <222> 26..88

<223> Vom Heijne matrix

score 4.4 seq AVASSFFCASLFS/AV

<221> polyA_signal <222> 755..760

<221> polyA_site <222> 775..787

-400- 111

<400> 111	
gacageetgg ataaaggete acttg atg get eag ttg gga gea gtt gtg get	52
Met Ala Gln Leu Gly Ala Val Ala	
-20 -15	
gtg get tee agt tte ttt tgt gea tet ete tte tea get gtg cac aag	100
Val Ala Ser Ser Phe Phe Cys Ala Ser Leu Phe Ser Ala Val His Lys	
-10 -5 1	148
ata gaa gag gga cat att ggg gta tat tac aga ggc ggt gcc ctg ctg Ile Glu Glu Gly His Ile Gly Val Tyr Tyr Arg Gly Gly Ala Leu Leu	140
5 10 15 20	
act tog acc age ggc cet ggt tto cat etc atg etc cet tto atc aca	196
Thr Ser Thr Ser Gly Pro Gly Phe His Leu Met Leu Pro Phe Ile Thr	
25 30 35	
tca tat aag tot gtg cag acc aca oto cag aca gat gag gtg aag aat	244
Ser Tyr Lys Ser Val Gln Thr Thr Leu Gln Thr Asp Glu Val Lys Asn	
40 45 50	
gta cot tgt ggg act agt ggt ggt gtg atg atc tac ttt gac aga att	292
Val Pro Cys Gly Thr Ser Gly Gly Val Met Ile Tyr Phe Asp Arg Ile	
55 60 65	240
gaa gtg gtg aac tte etg gte eeg aac gea gtg eat gat ata gtg aag	340
Glu Val Val Asn Phe Leu Val Pro Asn Ala Val His Asp Ile Val Lys	
10	388
aac tat act gct gac tat gac aag gcc ctc atc ttc aac aag atc cac Asn Tyr Thr Ala Asp Tyr Asp Lys Ala Leu Ile Phe Asn Lys Ile His	300
85 90 95 100	
cac gaa ctg aac cag ttc tgc agt gtg cac acg ctt caa gag gtc tac	436
His Glu Leu Asn Gln Phe Cys Ser Val His Thr Leu Gln Glu Val Tyr	
105 110 115	
att gag ctg ttt gga ctg gaa aat gat ttt tcc cag gaa tct tca	481
Ile Glu Leu Phe Gly Leu Glu Asn Asp Phe Ser Gln Glu Ser Ser	
120 125 130	
taaaagggac cctgagcaag aacatttttc atagcagaca ggaggactca tccacatcgc	541
cagcaatcat aattaagcaa accgcctttt gcaccattta agatttagga aatcatccaa	601
attactttta atgtttctgc agtagaaaat gaatctaaat tcattttata gggtttgtag	661 721
tottttatot gttttggatt cactgtgott ttaagaaaaa gttggtaaat ttgccgttga	781
tttttctttt taacctcaaa ctaatagaat tttataaaat attaattttc tccaaaaaaa	787
aaaaaa	, , ,

<210> 112

<211> 569

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 26..562

<221> sig_peptide

<222> 26..187

<223> Von Heijne matrix score 4.1

## seg AVVAAAARTGSEA/RV

<400> 112			
agaaacaggt ctgggctaca aaagt	atg gcc gct	tct gag gcg gcg	gtg gtg 52
	Met Ala Ala	Ser Glu Ala Ala	Val Val
		-50	
tot tog cog tot ttg aaa aca			
Ser Ser Pro Ser Leu Lys Thr	Asp Thr Ser	Pro Val Leu Glu	Thr Ala
-45 -40		-35	-30
gga acg gtc gca gca atg gct			
Gly Thr Val Ala Ala Met Ala		Ser Ala Arg Ala	Ala Ala
-25	-20		-15
gcg gtg gtt gcg gcc gcg gcc			
Ala Val Val Ala Ala Ala Ala		Ser Glu Ala Arg	Val Ser
-10	- 5	1	
aag gcc gct ttg gct acc aag			
Lys Ala Ala Leu Ala Thr Lys	Leu Leu Ser		Phe Ala
5 10		15	
gtg cac aag ccc aaa ggg ccc	_		
Val His Lys Pro Lys Gly Pro	Thr Ser Ala		_
20 25		30	35
aag gag aag ctg ctg gca gaa		▼ .	
Lys Glu Lys Leu Leu Ala Glu	Ala Gly Met	Pro Ser Pro Giu	50
40		cat aga aga act	
aag agg aaa aag cag act ttg Lys Arg Lys Lys Gln Thr Leu			•
55	60	65	neg wah
age gea gee ega gga gtt etg	• •		aca aaa 436
Ser Ala Ala Arg Gly Val Leu			
70	75	80	2,0
atg ttg acc agt atg ttg tca			att qqa 484
Met Leu Thr Ser Met Leu Ser			33
85 90	,,-	95	
gaa ctg ggg aaa gct act gat	aca cta gat	· ·	gta aca 532
Glu Leu Gly Lys Ala Thr Asp			
100 105		110	115
gaa gaa aaa cct tac ggt atg	aac ctc atc		569
Glu Glu Lys Pro Tyr Gly Met			
120	125		

<210> 113

<211> 893

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 4..810

<221> sig_peptide <222> 4..279

<223> Von Heijne matrix score 6.8 seq AVMLYTWRSCSRA/IP

<221> polyA_signal

<222> 858..863

<221> polyA_site <222> 881..893

<400	)> 11	. 3														
gcc	atg Met	atc Ile	Thr	cac His	gtc Val	acc Thr	ctg Leu	Glu	gat Asp	gcc Ala	ctg Leu	tcc Ser	aac Asn	gtg Val	gac Asp	48
			-90					-85					-80	~~~		0.6
													atc Ile			96
cca	cct		tcc	atc	ato	tac	_	act	aac	ttt	gac		aac	ttt	gag	144
													Asn			
													gag			192
	Arg	Asn	Ala	Phe		Thr	Gly	Ile	Ala		Tyr	Ile	Glu	Gln		
- 45					-40					-35				~~~	-30	240
aca	gtc	cac	CCC	agc	Mat	aat	Glu	Mer	Leu	Glu	Glu	Glv	cat His	Glu	Tyr	240
Int.	Val	nis	261	-25	MEC	Maii	Giu	riec	-20	GIU	GIU	Gry	114.5	-15	• / -	
aca	atc	atq	cta		acc	taa	cqc	agc		tcc	cgg	gcc	att		cag	288
Āla	Val	Met	Leu -10	Tyr	Thr	Trp	Arg	Ser	Cys	Ser	Arg	Ala	Ile 1	Pro	Gln	
gtg	aaa	tgc	aac	gag	cag	CCC	aac	cga	gta	gag	atc	tat	gag	aag	aca	336
	5	-				10					15		Glu			•••
gta	gag	gtg	ctg	gag	ccg	gag	gtc	acc	aag	ctc	atg	aag	ttc	atg	tat	384
Val 20	GIu	Val	Leu	Glu	Pro 25	GIU	vai	Thr	гув	30	Met	гÀг	Phe	met	35	
	cad	cac	aad	acc		gag	caa	ttc	tac		gag	ata	aag	caa		432
Phe	Gln	Arg	Lys	Ala 40	Ile	Glu	Arg	Phe	Cys 45	Ser	Glu	Val	Lys	Arg 50	Leu	
tgc	cat	gcc	gag	cgc	agg	aag	gac	ttt	gtc	tct	gag	gcc	tac	ctc	ctg	480
Суз	His	Ala	Glu 55	Arg	Arg	Lys	Asp	Phe 60	Val	Ser	Glu	Ala	Tyr 65	Leu	Leu	
acc	ctt	ggc	aag	ttc	atc	aac	atg	ttt	gct	gtc	ctg	gat	gag	cta	aag	528
		70					75					80	Glu			576
aac	atg	aag	tgc	agc	gtc	aag	aat	gac	cac	CCC	gcc	Tac	aag	agg	gca Ala	576
Asn	Met 85	rys	Cys	Ser	vai	Dys 50	Asn	Авр	HIB	ser	95	IYL	Lys	AIG	AIG	
aca		ttc	cta	caa	aaq		дса	gat	ccc	caq		atc	cag	gag	tcg	624
Ala	Gln	Phe	Leu	Arg	Lys	Met	Ala	Asp	Pro	Gln	Ser	Ile	Gln	Glu	Ser	
100					105					110					115	
cag	aac	ctt	tcc	atg	ttc	ctg	gcc	aac	caç	aac	agg	atc	acc	cag	tgt	672
Gln	Asn	Leu	Ser	Met 120		Leu	Ala	Asn	His 125		Arg	Ile	Thr	Gln 130		
ctc	cac	caq	caa	ctt	αaa	gtg	atc	cca	ggo	tat	gag	gag	ctg	ctg	gct	720
Leu	His	Gln	Gln	Leu	Ğlu	Val	Ile	Pro	Gly	Tyr	Glu	Glu	Lev	Lev	Ala	
			135					140					145	•		
gac	att	gtc	aac	atc	tgt	gtg	gat	tac	tac	gag	aac	: aag	ato	tac	ctg	768
Asp	Ile			Ile	Cys	Val			Tyr	Glu	Asr	Lys	Met	: Туз	Leu	
		150					155					160				810
act	CCC	agt	gag	aaa	cat	atg	CEC	CTC	aaç	y gra	i daā	1 CEC	CCC			010
inr			GIU	гÀа	nis	170		, nen	. by t	, va1	. Dys	. <u>.</u>	ı Pro	-		
tos	165	ac a	ccca	taas	ac c			וכ ככ	tcto	acct			catt	aaaa	aatccgt	870
	aaaa														-	893

<210> 114

<211> 1475

<212> DNA

<213> Homo sapiens

<220>

```
<221> CDS
<222> 55..459
<221> sig_peptide
<222> 55..120
<223> Von Heijne matrix
      score 7.2
      seq GLWLALVDGLVRS/SP
<221> polyA_signal
<222> 1444..1449
<221> polyA_site
<222> 1462..1475
<400> 114
                                                                    57
cagtteegea getacgtgtg ggaccegetg etgateetgt egeagategt eete atg
105
Gln Thr Val Tyr Tyr Gly Ser Leu Gly Leu Trp Leu Ala Leu Val Asp
                                          -10
                       -15
                                                                    153
ggg cta gtg cga agc agc ccc tcg ctg gac cag atg ttc gac gcc gag
Gly Leu Val Arg Ser Ser Pro Ser Leu Asp Gln Met Phe Asp Ala Glu
- 5
                   1
                                                                    201
atc ctg ggc ttt tee acc ect eca gge egg etc tee atg atg tee tte
Ile Leu Gly Phe Ser Thr Pro Pro Gly Arg Leu Ser Met Met Ser Phe
                               20
ate tte aac gee etc ace tgt gee etg gge ttg etg tac tte ate egg
                                                                    249
Ile Phe Asn Ala Leu Thr Cys Ala Leu Gly Leu Leu Tyr Phe Ile Arg
        30
                           35
cga gga aag cag tgt ctg gat ttc act gtc act gtc cat ttc ttt cac
                                                                    297
Arg Gly Lys Gln Cys Leu Asp Phe Thr Val Thr Val His Phe Phe His
                       50
   45
ctc ctg ggc tgc tgg ttc tac agc tcc cgt ttc ccc tcg gcg ctg acc
                                                                    345
Leu Leu Gly Cys Trp Phe Tyr Ser Ser Arg Phe Pro Ser Ala Leu Thr
                    65
tgg tgg ctg gtc caa gcc gtg tgc att gca ctc atg gct gtc atc ggg
Trp Trp Leu Val Gln Ala Val Cys Ile Ala Leu Met Ala Val Ile Gly
                                    85
gag tac ctg tgc atg cgg acg gag ctc aag gag ata ccc ctc aac tca
Glu Tyr Leu Cys Met Arg Thr Glu Leu Lys Glu Ile Pro Leu Asn Ser
                                100
gcc cct aaa tcc aat gtc tagaatcagg ccctttggac atcccgctga
Ala Pro Lys Ser Asn Val
        110
                                                                     549
cacttgggcc ccttaacacc ttgggctgct cagaccctcc agatgaggtc cagcccagat
ctgagaggaa ccctggaaat gtgaagtctc tgttggtgtg ggagagatag tgagggcctg
                                                                     609
                                                                     669
tcaaagaagg caggtagcag tcagcatgac agctgcaaga atgacctctg tctgttgaag
                                                                     729
cottggtato tgagaggtca ggaaggggac ctotttgagg gtaataacat aattggaaco
                                                                     789
atgccactct tgagccacaa tacctgtcac cagcctgttg ttttaagaga gaaaaaaat
                                                                     849
caaggatate tgattggage aaaccaette tttagteate tgtettaeet eeetgggaca
getgttacet ttgcagtgtt geegaateae ageagttace tttgcaatgt tgeegaatea
cagcagttct gttggagaaa cgcttggttt ccggatccag agccacagaa agaaatgtag
gtgtgaagta ttaggctgct gtcagggaga ggatggcaga tggaggcatc aagcacaagg
                                                                    1029
aaaatgcaca acctgtgccc tgttatacac acgttcatgt gcgcccaaga acctatgact
                                                                    1089
ttottocagt toottotaco aggtococat cotgotgoca gototoaaca tagoaggoca
                                                                    1149
taggacccag agaagaatcc cagtgttgct caaagtctga ccatcataaa gacactgcct
                                                                    1209
                                                                    1269
gtottotagg aatgaccagg cacccagete ceaetggact ceaatttttt tteetgeett
 atttagaatt ctttggcggg aagggtatga tgggttccca gagacaagaa gcccaacctt
                                                                    1329
                                                                    1389
 ctggcctggg ctgtgctgat agtgctgagg gagataggaa tttgctgcta agattttct
```

1449

ttggggtgga gtttcctctg tgaggggctt gcagctatcc ttcctgtgta tacaaataca

gtattttcca tgaaaaaaaa aaaaaa <210> 115 <211> 321 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 48..248 <221> sig_peptide <222> 48..161 <223> Von Heijne matrix score 6.3 seq LVFALVTAVCCLA/DG <221> polyA signal <222> 283..288 <221> polyA_site <222> 308..321 gctgagaaga gttgagggaa agtgctgctg ctgggtctgc agacgcg atg aat aac 56 Met Asn Asn 104 gtg cag ccg aaa ata aaa cat cgc ccc ttc tgc ttc agt gtg aaa ggc Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser Val Lys Gly -25 -30 -35 cac gtg aag atg ctg cgg ctg gtg ttt gca ctt gtg aca gca gta tgc 152 His Val Lys Met Leu Arg Leu Val Phe Ala Leu Val Thr Ala Val Cys -15 tgt ctt gcc gac ggg gcc ctt att tac cgg aag ctt ctg ttc aat ccc 200 Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu Phe Asn Pro 5 248 aac ggt cct tac cag aaa aag cct gtg cat gaa aaa aaa gaa gtt ttg Asn Gly Pro Tyr Gln Lys Lys Pro Val His Glu Lys Lys Glu Val Leu 25 20 tgattttata ttacttttta gtttgatact aagtattaaa catatttctg tattcttcca 308 321 aaaaaaaaa aaa <210> 116 <211> 450 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 25..399

<400> 116

<221> sig_peptide <222> 25..186

<223> Von Heijne matrix score 3.5

seq SILAQVLDQSARA/RL

ctgctccagc gctgacgccg agcc atg gcg gac gag gag ctt gag gcg ctg Met Ala Asp Glu Glu Leu Glu Ala Leu -50	51											
agg aga cag agg ctg gcc gag ctg cag gcc aaa cac ggg gat cct ggt Arg Arg Gln Arg Leu Ala Glu Leu Gln Ala Lys His Gly Asp Pro Gly -45 -35 -30	99											
gat gcg gcc caa cag gaa gca aag cac agg gaa gca gaa atg aga aac Asp Ala Ala Gln Gln Glu Ala Lys His Arg Glu Ala Glu Met Arg Asn -25 -20 -15	147											
agt atc tta gcc caa gtt ctg gat cag tcg gcc cgg gcc agg tta agt Ser Ile Leu Ala Gln Val Leu Asp Gln Ser Ala Arg Ala Arg Leu Ser -10 -5 1	195											
aac tta gca ctt gta aag cct gaa aaa act aaa gca gta gag aat tac Asn Leu Ala Leu Val Lys Pro Glu Lys Thr Lys Ala Val Glu Asn Tyr 5 10	243											
ctt ata cag atg gca aga tat gga caa cta agt gag aag gta tca gaa Leu Ile Gln Met Ala Arg Tyr Gly Gln Leu Ser Glu Lys Val Ser Glu 20 25 30	291											
caa ggt tta ata gaa atc ctt aaa aaa gta agc caa caa aca gaa aag Gln Gly Leu Ile Glu Ile Leu Lys Lys Val Ser Gln Gln Thr Glu Lys 40 45 50	339											
aca aca aca gtg aaa ttc aac aga aga aaa gta atg gac tct gat gaa Thr Thr Thr Val Lys Phe Asn Arg Arg Lys Val Met Asp Ser Asp Glu 55 60 65	387											
gat gac gat tat tgaactacaa gtgctcacag actagaactt aacggaacaa Asp Asp Asp Tyr 70	439											
gtctaggaca g	450											
<210> 117 <211> 1173 <212> DNA <213> Homo sapiens												
<220> <221> CDS <222> 101137												
<221> sig_peptide <222> 10.72 <223> Von Heijne matrix score 6.5 seq_LLTLLLPPPPLYT/RH												
<221> polyA_signal												
<221> polyA_site <222> 11621173												
<pre>&lt;400&gt; 117 gagctgctt atg gga cac cgc ttc ctg cgc ggc ctc tta acg ctg ctg ct Met Gly His Arg Phe Leu Arg Gly Leu Leu Thr Leu Leu Leu -20 -15 -10</pre>	g 51 u											
ccg ccg cca ccc ctg tat acc cgg cac cgc atg ctc ggt cca gag tcc Pro Pro Pro Pro Leu Tyr Thr Arg His Arg Met Leu Gly Pro Glu Ser	99											
gtc ccg ccc cca aaa cga tcc cgc agc aaa ctc atg gca ccg ccc cga Val Pro Pro Pro Lys Arg Ser Arg Ser Lys Leu Met Ala Pro Pro Arg 10 20 25	147											

WO 99/31236 -92 - PCT/IB98/02122

								cac His								195
gca Ala	ctg Leu	ctt Leu	cgc Arg 45	ctc Leu	ctg Leu	ccg Pro	gag Glu	tac Tyr 50	cgg Arg	gat Asp	gca Ala	gag Glu	att Ile 55	gtg Val	cgg Arg	243
acc Thr	cgg Arg	gat Asp 60	ccc	gaa Glu	aaa Lys	ctc Leu	gct Ala 65	tcc Ser	tgt Cys	gac Asp	atc Ile	gtg Val 70	gtg Val	gac Asp	gtg Val	291
G1A aaa	ggc Gly 75	gag	tac Tyr	gac Asp	cct Pro	cgg Arg 80	aga	cac His	cga Arg	tat Tyr	gac Asp 85	cat His	cac His	cag Gln	agg Arg	339
tct Ser 90	ttc	aca Thr	gag Glu	acc Thr	atg Met 95	agc Ser	tcc Ser	ctg Leu	tcc Ser	cct Pro 100	ggg Gly	agg Arg	ccg Pro	tgg Trp	cag Gln 105	387
acc	aag Lys	ctg Leu	agc Ser	agt Ser 110	gcg	gga Gly	ctc Leu	atc Ile	tat Tyr 115	ctg Leu	cac His	ttc Phe	ggg Gly	cac His 120	aag Lys	435
ctg L <b>e</b> u	ctg Leu	gcc Ala	cag Gln 125	ttg	ctg Leu	ggc Gly	act Thr	agt Ser 130	gaa Glu	gag Glu	gac Asp	agc Ser	atg Met 135	gtg Val	ggc Gly	483
acc Thr	ctc Leu	tat Tyr 140	qac	aag Lys	atg Met	tat Tyr	gag Glu 145	aac Asn	ttt Phe	gtg Val	gag Glu	gag Glu 150	gtg Val	gat Asp	gct Ala	531
gtg Val	gac Asp 155	aat	ggg Gly	atc Ile	tcc Ser	cag Gln 160	tgg	gca Ala	gag Glu	ggg Gly	gag Glu 165	cct Pro	cga Arg	tat Tyr	gca Ala	579
ctg Leu 170	acc	act Thr	acc Thr	ctg Leu	agt Ser 175	gca	cga Arg	gtt Val	gct Ala	cga Arg 180	ctt Leu	aat Asn	cct Pro	acc Thr	tgg Trp 185	627
aac	cac His	ccc Pro	gaç Asp	caa Gln 190	gac	act Thr	gag Glu	gca Ala	999 Gly 195	ttc Phe	aag Lys	cgt Arg	gca Ala	atg Met 200	Asp	675
ctg Leu	gtt Val	caa Gln	gag Glu 205	gag	ttt Phe	ctg Leu	cag Gln	aga Arg 210	tta	gat Asp	ttc Phe	tac Tyr	caa Gln 215	His	agc Ser	723
tgg Trp	ctg Leu	cca Pro 220	qcc	cgg Arg	gcc Ala	ttg Leu	gtg Val 225	gaa	gag Glu	gcc Ala	ctt Leu	gcc Ala 230	cag Gln	cga Arg	ttc Phe	771
cag Gln	gtg Val 235	qac	cca Pro	agt Ser	gga Gly	gag Glu 240	att	gtg Val	gaa Glu	ctg Leu	gcg Ala 245	Lys	ggt Gly	gca Ala	tgt Cys	819
ccc Pro 250	tag	aag Lys	gag Glu	cat His	ctc Leu 255	tac	cac His	ctg Leu	gaa Glu	tct Ser 260	Gly	ctg Leu	tcc Ser	cct Pro	cca Pro 265	867
ata	gcc Ala	atc Ile	ttc Phe	ttt Phe 270	gtt Val	atc Ile	tac Tyr	act Thr	gac Asp 275	cag Gln	gct	gga Gly	cag Glr	tgg Trp 280	g cga Arg	915
ata Ile	cag Gln	tg <b>t</b> Cys	gtg Val 285	ccc Pro	aag	gag Glu	ccc	cac His	tca Ser	tto	caa Glr	ago Ser	cgg Arg 299	Le	g ccc u Pro	963
ctg Leu	cca Pro	gag Glu 300	cca Pro	tgg	cgg Arg	ggt	ctt Leu 305	cgg Arg	gac	gaç Glu	g gco	c cto Lev	ı Ası	c, caq o Gli	g gtc n Val	1011
agt Ser	Gly	atc	cct	ggc	tgc Cys	ato Ile	ttc Phe	gtc	cat . His	gca Ala	a ago a Se:	gg c Gly	tt:	e Il	t ggc e Gly	1059
Gly	His	cac	acc Thr	cga Arg	gag Glu 335	ggt	gco	ttç Lei	ago Sei	atq r Mei 340	g gc	c cgi	g Al	c ac a Th	c ttg r Leu 345	1107
330 gcc Ala	cag	cgc	tca Ser	tac Tyr	cto		caa Glr	a ato	tco Se:	ta:		aata	aaa	cctt		1157

tctcaaaaaa aaaaaa

350

355

1173

<210> 118 <211> 785 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 72..704 <221> sig_peptide <222> 72..161 <223> Von Heijne matrix score 13.2 seg LLLLSTLVIPSAA/AP <221> polyA_signal <222> 772..777 <400> 118 cggaatccgg gagtccggtg acccgggctg tggtctagca taaaggcgga gcccagaaga 60 aggggcgggg t atg gga gaa gcc tcc cca cct gcc ccc gca agg cgg cat 110 Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His -25 ctg ctg gtc ctg ctg ctc ctc tct acc ctg gtg atc ccc tcc gct 158 Leu Leu Val Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala -10 -15 gea get cet ate cat gat get gae gee caa gag age tee ttg ggt ete 206 Ala Ala Pro Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu 10 aca ggc ctc cag agc cta ctc caa ggc ttc agc cga ctt ttc ctg aaa 254 Thr Gly Leu Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys 25 20 ggt aac ctg ctt cgg ggc ata gac agc tta ttc tct gcc ccc atg gac 302 Gly Asn Leu Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp 40 ttc cgg ggc ctc cct ggg aac tac cac aaa gag gag aac cag gag cac 350 Phe Arg Gly Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His 55 50 cag ctg ggg aac aac acc ctc tcc agc cac ctc cag atc gac aag gta 398 Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val 70 ccc agg atg gag gag gag gcc ctg gta ccc atc cag aag gcc acg 446 Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr 85 80 gac age tte cac aca gaa ete cat eee egg gtg gee tte tgg ate att 494 Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile 105 100 aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac 542 Lys Leu Pro Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His 125 120 115 tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc 590 Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu 140 135 cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tec 638 Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser 150 155 145 tee eac tee agg etg tee eec ega aag ace cae tta etg tae ate etc 686

Ser His Ser Arg Leu Ser Pro Arg Lys Thr His Leu Leu Tyr Ile Leu 160 165 170 175	•
agg ccc tct cgg cag ctg taggggtggg gaccggggag cacctgcctg Arg Pro Ser Arg Gln Leu	734
180 tagcccccat cagaccctgc cccaagcacc atatggaaat aaagttcttt c	785
<210> 119	
<211> 559	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 44505	
<221> sig_peptide	
<222> 44223	
<223> Von Heijne matrix	
score 4 seq_LVRRTLLVAALRA/WM	
564 2 · · · · · · · · · · · · · · · · · ·	
<400> 119	55
agcaaccaga gggagatgat cacctgaacc actgctccaa acc atg ggc agt aaa Met Gly Ser Lys -60	33
tgc tgt aaa ggt ggt cca gat gaa gat gca gta gaa aga cag agg cgg	103
Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu Arg Gln Arg	
-55 -50 -45 cag aag ttg ctt ctt gca caa ctg cat cac aga aaa agg gtg aag gca	151
Gln Lys Leu Leu Ala Gln Leu His His Arg Lys Arg Val Lys Ala	
-40 -35 -30 -25	
get ggg cag ate cag gee tgg tgg egt ggg gte etg gtg ege agg ace	199
Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu Val Arg Arg Thr	
-20 -15 -10	247
ctg ctg gtt gct gcc ctc agg gcc tgg atg att cag tgc tgg tgg agg	24,
Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln Cys Trp Trp Arg	
aco tto oto cao aga coo atc cot cao coo coo cao occ cto tto ago	295
Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln Ala Leu Leu Arg	
10 15 20	343
gto tac gto ato cag gag cag gcg acg gto aag cto cag too tgc ato	343
Val Tyr Val Ile Gln Glu Gln Ala Thr Val Lys Leu Gln Ser Cys Ile	
25 30 35 40 cgc atg tgg cag tgc cgg caa tgt tac cgc caa atg tgc aat gct ctc	391
Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met Cys Asn Ala Leu	
45 50 55	
tgc ttg ttc cag gtc cca gag agc agc ctt gcc ttc cag act gat ggc	439
Cys Leu Phe Gln Val Pro Glu Ser Ser Leu Ala Phe Gin Thr Asp Gly	
60 65 70	487
ttt tta cag gtc caa tat gca atc cct tca aag cag cca gag ttc cac	
Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln Pro Glu Phe His 80 85	
75 80 85 att gaa atc cta tca atc tgaaaggcct ggggcatgga gaacaggctg	535
Ile Glu Ile Leu Ser Ile	
90	
cactacceta ataaatgtet gace	559

```
<210> 120
<211> 770
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 25..393
<221> sig_peptide
<222> 25..150
 <223> Von Heijne matrix
      score 4.6
     seq LDPAVSLSAPAFA/SA
 <221> polyA_signal
 <222> 734..739
 <221> polyA site
 <222> 757..770
 <400> 120
                                                                       51
 cgcagaaagg agagacacac atac atg aaa gga gga gct ttc tcc aat ctt
                            Met Lys Gly Gly Ala Phe Ser Asn Leu
                                    -40
 aat gat tee cag ete tea gee teg ttt etg caa eee age etg caa gea
                                                                       99
Asn Asp Ser Gln Leu Ser Ala Ser Phe Leu Gln Pro Ser Leu Gln Ala
                                                     -20
                                 -25
             -30
                                                                      147
 aac tgt cet get ttg gac eet get gtg tea ete tee gea eea gee ttt
 Asn Cys Pro Ala Leu Asp Pro Ala Val Ser Leu Ser Ala Pro Ala Phe
                                                 -5
                            -10
 gee tet get ett ege tet atg aag tee tee cag get gea egg aag gae
                                                                      195
 Ala Ser Ala Leu Arg Ser Met Lys Ser Ser Gln Ala Ala Arg Lys Asp
                                         10
 gac ttt ctc agg tct ctt agt gat gga gac tca ggg aca tca gaa cac
                                                                      243
 Asp Phe Leu Arg Ser Leu Ser Asp Gly Asp Ser Gly Thr Ser Glu His
                                     25
                 20
 atc tca gcg gtg gtg act agc cct cgg att tcc tgc cat ggt gct gcc
                                                                       291
 Ile Ser Ala Val Val Thr Ser Pro Arg Ile Ser Cys His Gly Ala Ala
                                 40
            35
 att ecc acc gec egt gec etc tge eta gge tgt tee tge tge acc gaa
                                                                       339
 Ile Pro Thr Ala Arg Ala Leu Cys Leu Gly Cys Ser Cys Cys Thr Glu
                            55
 ege etc etc etg eca eeg ecc tec etc ett tet tta gaa gee eet gee
                                                                       387
 Arg Leu Leu Pro Pro Pro Ser Leu Leu Ser Leu Glu Ala Pro Ala
                                             75
                                                                       443
 ago aco tgagetetet getgattget gtteetecca gtetgtggaa getttgeeca
 Ser Thr
 80
                                                                       503
 tatgetttee ttaaaagggt tetgggeagg geaggegeee ceatttetea gggateeeet
                                                                       563
 ccaggacaac gccttttcct tgtgtcttca gctctcctta ccagatatct atatatttgt
 atatattcag tttcaccaac aatgcatcaa gtactttttt ttttaagtaa agaaccgcag
                                                                        623
 toategaact ggageeccat tgattecete eccetegeet ecceaaatet ggeacetgee
                                                                        683
 caaggtatee teagaaceat tiggggtgte ettiggeatt ggataataga aataaaattt
                                                                        743
                                                                        770
 tacctctttc tacaaaaaaa aaaaaac
```

<210 > 121 <211 > 1213

<212> DNA

<213 > Homo sapiens

WO 99/31236 -96 - PCT/IB98/02122

<220 <221 <222	> CD		95													
<221 <222	> si > 58 > Vo	g_pe 11 n He	ptid 4 ijne		rix											
		ore q LS	5.4 HLLP	SLRQ	VIQ/	EP										
	-		site 1213													
<400	> 12	1							<b>-</b>			a > <b>a a</b>		2020	cc	57
cctg	gctt	tg c	cttt	gccc	t gc	tgtg ctc	tgat	CET	agct ctc	ccc	cca	caggo agt	cta :	acag cga	caq	105
Met	Ala	Met	Ala	Gln -15	Lys	Leu	Ser	His	Leu -10	Leu	Pro	Ser 1	Leu	Arg -5	31n	
gtc	atc	cag	gag	cct	cag	cta	tct	ctg	cag	cca	gag	cct	gtc	ttc	acg	153
Val	Ile	Gln		Pro	Gln		Ser 5	Leu	Gln	Pro	Glu	Pro	Val	Pne	Inr	
ata	gat	саа	1 act	gag	qtg	cca	ccq	ctc	ttc	tgg	aag	ccg	tac	atc	tat	201
Val	Asp	Arg	Ala	Glu	Val	Pro 20	Pro	Leu	Phe	Trp	Lys 25	Pro	Tyr	11e	ıyr	242
gcg	ggc	tac	cgg	ccg	ctg	cat	cag	acc	tgg	cgc	ttc	tat	ttc	cgc	acg Thr	249
	Gly	Tyr	Arg	Pro	Leu 35	His	GIN	Thr	Trp	Arg	Pne	Tyr	FILE	Arg	45	
30 cta	ttc	cag	cad	cac	aac	gag	gcc	gtg	aat	gtc	tgg	acc	cac	ctg	ctg	297
Leu	Phe	Gln	Gln	His	Asn	Ğlü	Ala	Val	Asn	Val	Trp	Thr	His	Leu	Leu	
				50					55					60		345
gcg	gcc	ctg	gta	ctg	ctg	ctg	cgg	Leu	Ala	Leu	Phe	gtg Val	Glu	Thr	Val	• • • • • • • • • • • • • • • • • • • •
			65					70					/5			
gac	ttc	tgg	~~=	gac	cca	cac	gcc	ctg	CCC	ctc	ttc	atc	att	gtc	ctt	393
Asp	Phe	Trp	Gly	Asp	Pro	His	Ala	Leu	Pro	Leu	Phe	Ile 90	ITE	vaı	Leu	
	<b>-</b>	80	300	t a C	ctc	tcc	85 ctc	agt	acc	tta	act	cac	ctc	ctg	cag	441
gcc Ala	Ser	Phe	Thr	TVY	Leu	Ser	Leu	Ser	Ala	Leu	Ala	His	Leu	Leu	Gln	
	95					100					105					489
gcc	aag	tct	gag	ttc	tgg	cat	tac	agc	ttc	ttc	ttc	ctg	gac	TVY	Val	407
	Lys	Ser	Glu	Phe	115	HIS	Tyt	261	Pile	120	FIIC	Leu	no p	-1-	125	
110	ata	acc	ata	tac	cag	ttt	ggc	agt	gcc	ttg	gca	cac	ttc	tac	tat	537
Gly	Val	Ala	Val	Tyr	Gln	Phe	Gly	Ser	Ala	Leu	Ala	His	Phe	Tyr	TAT	
				130					135					140		585
gct	atc	gag	CCC	gcc	tgg	His	Ala	Gln	Val	Gln	. Ala	gtt Val	Phe	Leu	Pro	
			145					150					155			
atg	gct	gcc	ttt	ctc	gcc	tgg	ctt	tcc	tgo	att	ggc	tcc	tgo	tat	aac	633
Met	Ala	Ala	Phe	Leu	Ala	Trp	Leu 165	Ser	Суз	ille	: GI	170	Cys	ıyı	ASII	681
aag	tac	ato	cag	aaa	cca	ggc	ctg	ctg	ggo	cgo	aca Th	a tgc	Cac	gay Gli	g gtg	001
	175					180					18:	5			ı Val	
ccc	+00	arc	ctg	gcc	tac	αca	cta	gac	att	agt	. cc1	gtg	gt	cat	cgt	729
Pro	Ser	Val	Leu	Ala	Tyr	Ala	Leu	. Asp	Ile	e Sei	Pro	o Val	. Val	L H1	a Arg	
190	, .				195				יבה ז	200 F gat		a act	cti	c ct		777
atc	tto	gto	CAY	CCC Ser	gac Asr	Pro	Thr	Thi	Ası	p Asi	o Pr	o Ala	Le	ı Le	c tac u Tyr	
				210	)				21	5				42	U	005
cac	aag	tgo	cag	gte	gto	tto	ttt	ct	ct	g gc	r gc	t gco	: tt	c tt	c tct	825

WO 99/31236 -97- PCT/IB98/02122

His Lys Cys Gln Val Val Phe Phe Leu Leu Ala Ala Phe Phe Ser	
225 230 235	
acc ttc atg ccc gag cgc tgg ttc cct ggc agc tgc cat gtc ttc ggg	873
Thr Phe Met Pro Glu Arg Trp Phe Pro Gly Ser Cys His Val Phe Gly	
240 245 250	
210	921
cag ggc cac caa ctt ttc cat atc ttc ttg gtg ctg tgc acg ctg gct	,,,
Gln Gly His Gln Leu Phe His Ile Phe Leu Val Leu Cys Thr Leu Ala	
255 260 265	0.50
cag ctg gag gct gtg gca ctg gac tat gag gcc cga cgg ccc atc tat	969
Gln Leu Glu Ala Val Ala Leu Asp Tyr Glu Ala Arg Arg Pro Ile Tyr	
270 275 280 285	
gag cot org cac acg cac tgg cot cac aac tit tot ggc ore tite org	1017
Glu Pro Leu His Thr His Trp Pro His Asn Phe Ser Gly Leu Phe Leu	
250	1065
ctc acg gtg ggc agc agc atc ctc act gca ttc ctc ctg agc cag ctg	1003
Leu Thr Val Gly Ser Ser Ile Leu Thr Ala Phe Leu Leu Ser Gln Leu	
305 310 315	
gta cag cgc aaa ctt gat cag aag acc aag tgaaggggga tggcatctgg	1115
Val Gln Arg Lys Leu Asp Gln Lys Thr Lys	
320 325	
tagggaggga ggtatagttg ggggacaggg gtctgggttt ggctccaagt gggaacaagg	1175
tagggaggga ggtatagttg ggggataggg gtttagttt ggtttagt gggtatagtt	1213
cctggtaaag ttgtttgtgt ctggccaaaa aaaaaaaa	
<210> 122	
<211> 1318	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 31660	
221. sig popride	
<221> sig_peptide	
<222> 3190	
<222> 3190   <223> Von Heijne matrix	
<222> 3190	
<222> 3190   <223> Von Heijne matrix	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix score 5.4</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix     score 5.4     seq AFVIACVLSLIST/IY</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix     score 5.4     seq AFVIACVLSLIST/IY &lt;221&gt; polyA_signal</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix     score 5.4     seq AFVIACVLSLIST/IY</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix     score 5.4     seq AFVIACVLSLIST/IY &lt;221&gt; polyA_signal</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	54
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	54
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	54
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	54
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102 150 198
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102 150 198
<pre>&lt;222&gt; 3190 &lt;223&gt; Von Heijne matrix</pre>	102 150 198

															350	294
ggc	aca	gtg	gga	ttg	tgg	aga	cgg	tgt	atc	acc	ata	CCC	aaa	aac aac	Mar	234
Gly	Thr	Val	Gly	Leu	Trp	Arg	Arg	Cys	TIE	Thr	He	Pro	Lys	ASII	Met	
		55					60					65			202	342
cat	tgg	tat	agd	cca	cca	gaa	agg	aca	gag	tca	ttt	gat	gcg	y	The	372
His	Trp	Tyr	Ser	Pro	Pro	Glu	Arg	Thr	GIA	Ser	Pne	Asp	Vai	Val	1111	
	70					75					80				art	390
aaa	tgt	gtg	agt	ttc	aca	cta	act	gag	cag	בבכ	atg	gag	dad	Dho	yet val	3,50
Lys	Cys	Val	Ser	Phe		Leu	Thr	GIU	Gin	Pne	Met	GIU	гуѕ	Pne	100	
85					90					95						438
gat	CCC	gga	aac	cac	aat	agc	333	att	gat	ctc	CEE	agg	acc	Tat	Tou	430
Asp	Pro	Gly	Asn	His	Asn	Ser	Gly	Ile	Asp	Leu	Leu	Arg	Thr	Tyr	Leu	
				105					110					115		486
tgg	cgt	tgc	cag	ttc	ctt	tta	cct	ttt	gtg	agt	tta	ggt	ttg	atg	tgc	400
Trp	Arg	Cys	Gln	Phe	Leu	Leu	Pro	Phe	Val	Ser	Leu	Gly	Leu	Met	Cys	
			120					125					130			534
ttt	999	gct	ttg	atc	gga	ctt	tgt	gct	tgc	att	tgc	cga	agc	tta	tat	534
Phe	Gly	Ala	Leu	Ile	Gly	Leu	Суз	Ala	Cys	Ile	Суз	Arg	Ser	Leu	TYE	
		135					140					145				
ccc	acc	att	gcc	acg	ggc	att	ctc	cat	ctc	ctt	gca	gtg	aca	aag	gag	582
Pro	Thr	Ile	Ala	Thr	Gly	Ile	Leu	His	Leu	Leu	Ala	vaı	Thr	Lys	Glu	
	150					155					160					<b>600</b>
agc	atq	ctt	cca	gct	gga	gct	gag	tcc	aag	cac	aca	gcc	act	cct	gca	. 630
Ser	Met	Leu	Pro	Ala	Gly	Ala	Glu	Ser	Lys	His	Thr	Ala	Thr	Pro	ALG	
165					170					175					100	
cac	qca	tac	gtg	caa	aca	<b>999</b>	aag	ccc	aag	tag	gaga	aga	ggaa	agag	gt	680
His	Ala	Cys	Val	Gln	Thr	Gly	Lys	Pro	Lys							
				185					190	1						
tat	aggg	att	tggg	aaga	ac c	ttga	ttat	t co	ctgg	agga	aaa	igaca	laat	ctac	ttccct	740
722	atca	CCC	trga	atct	ac t	tcca	ccct	c ac	aact	taaa	ı atç	jaact	.gca	LCC		800
cat	cttc	+++	FCFF	ctcc	ag t	gaat	atqa	it ct	ccaa	lacco	: ככ	ובבבו	CCC		gaactyt	860
222	attt	cca	CECA	taga	ca a	taca	acca	ia ca	igato	caat	: Ctc	gaç	gaag	acyc	idaatty	920
772	cctc	tta	ttat	aaaa	itt a	acct	agct	g ga	ictca	ıggaa	a acc	aggg	gaag	aay	caacyc	980
200	catt	taa	aato	taaa	at t	tttt	ctgo	gt ta	aato	ctatt	tai	יבבבי	CCL	yeas	99009	1040
	++~+	t.c.c	Cagt	++++	ct c	ictct	aato	at al	aaca	aaaca	a ggv	caa	aatt	CCC	Jacobs	1100
	coto	2+2	OT ac	ttaa	at c	ctac	ctto	ac at	acti	caato	g cai	cagt	gaaa	cgg	cattlag	1160
		202	Cacc	ccca	aa a	caca	accad	cc at	tttca	attag	g gt	gccc	aada	aat	ccegcae	1220
tta	actt	att	tatt	tatt	at t	att	ttg	ct t	tttc	taad	c cc	acta	tata	ttg	actgcaa	1280
200	aatt	aat	aaat	tato	cac t	tct	ggaā	aa a	aaaa	aaa						1318
~~9						•										

```
<210> 123
```

<213> Homo sapiens

<220>

<221> CDS

<222> 31..582

<221> sig_peptide <222> 31..90

<223> Von Heijne matrix score 5.4 seq AFVIACVLSLIST/IY

<221> polyA_signal

<222> 816..821

<221> polyA_site <222> 840..853

<211> 853

<212> DNA

<400> ggagg	12:	3 39 C	gage	agte	t ga	atgc	caga	atg	gat	aac	cgt	ttt	gct	aca	gca	54
								- 20	vsħ	73			-15			
ttt 9	ata :	att	act	tqt	gtg	ctt	agc	ctc	att	tcc	acc	atc	tac	atg	gca	102
Phe V	Val	Ile	Ala	Cys	Val	Leu	5er -5	rea	116	361		1	-1-			
gcc t			aac	aca	gac	ttc	tgg	tat	gaa	tat	cga	agt	cca	gtt	caa	150
gcc ( Ala S	Ser	Tle	Glv	Thr	Asp	Phe	Trp	Tyr	Glu	Tyr	Arg	Ser	Pro	Val		
-					10					7.3						
	aat	tee	agt	gat	tta	aat	aaa	agc	atc	tgg	gat	gaa	ttc	att	agt	198
gaa a Glu i	Δen	Ser	Ser	Asp	Leu	Asn	Lys	Ser	Ile	Trp	Asp	Glu	Phe		Ser	
				26					30							2.6
gat	~aa	aca	gat		aaσ	act	tat	aat	gat	gca	cct	ttt	cga	tac	aat	246
gat (	Glu	Ala	Asp	Glu	Lvs	Thr	Tyr	Asn	Asp	Ala	Pro	Phe	Arg	Tyr	Asn	
ggc	202	cta		tta	taa	aqa	cgg	tgt	atc	acc	ata	CCC	aaa	aac	atg	294
ggc Gly	Thr	Val	Glv	Leu	Trp	Arq	Arg	Cys	Ile	Thr	Ile		Lys	Asn	Mec	
																340
cat	taa		agc	cca	cca	gaa	agg	aca	gag	tca	ttt	gat	gtg	gtc	aca .	342
cat His	Tro	Tvr	Ser	Pro	Pro	Glu	Arg	Thr	Glu	Ser		Asp	Val	Val	Thr	
						75										390
		ata	agt	ttc	aca	cta	act	gag	cag	ttc	atg	gag	aaa	CEE	gtt	330
aaa Lys	Cvs	Val	Ser	Phe	Thr	Leu	Thr	Glu	Gln	FILE	Met	Glu	rys	Pne	val	
					00					22						438
	ccc	qqa	aac	cac	aat	agc	999	att	gat	ctc	ctt	agg	acc	tat	ctt Leu	430
Asp	Pro	Glv	Asn	His	Asn	Ser	Gly	Ile	Asp	Leu	Leu	Arg	Thr	lyr		
																486
taa	cat	tac	caq	ttc	ctt	tta	cct	ttt	gto	gagt	tta	ggt	ttg	atg	tgc Cys	400
Tro	Ara	Cvs	Gln	Phe	Leu	Leu	Pro	Phe	· Val	Ser	Leu	Gly	Leu	met	Cys	
																534
ttt	aga	qct	ttg	atc	gga	ctt	tgt	gct	tg:	att	: tgc	: cga	ago	T CL	tat Tyr	33.
Phe	Gly	Ala	Leu	Ile	Gly	/ Lev	Cys	Ala	ı Cys	3 Ile	Cys		•	שבי	Tyr	
																582
ccc	acc	att	gco	acg	ggg	att	cto	cat	ct	c ctt	gca	a gat	acc	. all	g ctg : Leu	50-
Pro	Thr	Ile	Ala	Thr	Gly	/ Ile	e Lev	ı His	s Le	u Lei	4 7.1.		) Ini	Me	Leu	
																642
tga	agto	cag	gcca	acato	ga g	ggtgi	tact	gt gi	taga	tgct	c ca	getg	aaat		aagctaa atgtcca	_
act	ctaa	ıtaa	agaa	accaa	act .	agct	gage	cc a	acca	acct	a tg	gaac	cgat	aya	aataaaa	85
tga	atte	ittg	ttt	tgcga	aaa	aaaa	aaaa	aa a								,,,,
	-	_														

<210> 124

<211> 826

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 15..695

<221> sig_peptide <222> 15..80

<223> Von Heijne matrix score 8.5 seq AALLLGLMMVVTG/DE

<221> polyA_signal <222> 795..800

<221>	polyA_site
<222>	814826

aac	caga	ggt	gccc													
				мес	GIÀ	-20	Thr	мес	Arg	Leu	-15	Thr	Ala	Ala	Leu	
tta	ctg	ggt	ctc	atg	atg	gtg	gtc	act	gga	gac	gag	gat	gag	aac	agc	
Leu -10	Leu	Gly	Leu	Met	Met -5	Val	Val	Thr	Gly	Asp 1	Glu	Asp	Glu	Asn 5	Ser	
														tgc		1
			10					15					20	Cys		
ggc	ctt	gaa	gtt	ttc	tac	cca	gag	ttg	999	aac	att	ggc	tgc	aag	gtt	1
		25					30					35		Lys		
_							_		-					atg		2
	40	_				45	_		-		50		-	Met		
														atc		2
55	iie	vaı	ràs	Pne	60	GIY	Ата	vai	Asp	65	Ala	Thr	туг	Ile	Jeu 70	
	ato	ata	gat	cca		acc	cct	agc	aga		gaa	ccc	aga	cag		3
	-		_		-	_		_	-	-	_		_	Gln 85	_	
ttc	tgg	aga	cat	tgg	ctg	gta	aca	gat	atc	aag	ggc	gcc	gac	ctg	aag	3
Phe	Trp	Arg	His 90	Trp	Leu	Val	Thr	Asp 95	Ile	Lys	Gly	Ala	Asp 100	Leu	Lys	
		_		_		_				-		_	-	ccc		4
_	_	105			-		110				-	115		Pro		
	_	_		-				_		_			_	tat		4
	120				•	125		-	•		130			Tyr		
_	-		_	_						_	-			act	-	5
135		_	_		140					145			_	Thr	150	
ggc	tct	tgg	aaa	atg	gac	aga	ttt	ctg	aac	cgt	ttc	cac	ctg	ggc	gaa	5
				155					160					Gly 165		
														tca		•
			170					175					180	Ser		
														aaa		•
		185					190					195		Lys		
_				_	_	_	tag	atag	ccg	gctt	tgcc	at c	cggg	catg	t	,
Gln	Ala 200	Glu	Ile	Ala	Ala	Cys 205										

<210> 125

<211> 571

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

WO 99/31236 -101- PCT/IB98/02122

```
<222> 74..295
<221> sig_peptide
<222> 74..196
<223> Von Heijne matrix
      score 5.4
      seq RLLYIGFLGYCSG/LI
<221> polyA signal
<222> 545..550
<221> polyA_site
<222> 561..571
<400> 125
cgggtagtgg tcgtcgtggt tttccttgta gttcgtggtc tgagaccagg cctcaagtgg
                                                                      60
aaacggcgtc acc atg atc gca cgg cgg aac cca gta ccc tta cgg ttt
                                                                     109
               Met Ile Ala Arg Arg Asn Pro Val Pro Leu Arg Phe
                   -40
                                       -35
ctg ccg gat gag gcc cgg agc ctg ccc ccg ccc aag ctg acc gac ccg
                                                                     157
Leu Pro Asp Glu Ala Arg Ser Leu Pro Pro Pro Lys Leu Thr Asp Pro
                -25
cgg ctc ctc tac atc ggc ttc ttg ggc tac tgc tcc ggc ctg att gat
                                                                     205
Arg Leu Leu Tyr Ile Gly Phe Leu Gly Tyr Cys Ser Gly Leu Ile Asp
                                -5
            -10
aac ctg atc cgg cgg agg ccg atc gcg acg gct ggt ttg cat cgc cag
                                                                      253
Asn Leu Ile Arg Arg Pro Ile Ala Thr Ala Gly Leu His Arg Gln
                        10
                                            15
ctt cta tat att acg gcc ttt ttt ttg ctg gat att atc ttg
                                                                     295
Leu Leu Tyr Ile Thr Ala Phe Phe Leu Leu Asp Ile Ile Leu
                    25
taaaacgtga agactacctg tatgctgtga gggaccgtga aatgtttgga tatatgaaat
tacatccaga ggattttcct gaagaagata agaaaacata tggtgaaatt tttgaaaaaat
                                                                      415
                                                                      475
tocatocaat acgttgaagt ottoaaaatg ottgotocag titoactgat acctgotgtt
                                                                      535
cctgaatttg atggaacatg tttcttatga cagttgaagc ttatgctaat ctgtatgttg
acaccttgta attaaaatac gtaccaaaaa aaaaaa
<210> 126
<211> 659
<212> DNA
<213> Homo sapiens
<221> CDS
<222> 440..658
<221> polyA_signal
<222> 601..606
<400> 126
cgccttacga gctgggaggt ggtgcctctc acccagctaa ttgctctcta gcccttggcc
                                                                       60
ttcacaggtg ttggtgcctg ccgtgaacgc attctgacct gggccgtatc tgtctcccaa
                                                                      120
                                                                      180
gactttgtgc ctatggttgg ggacagagtg aggtcgttgc cttgacgacg acagcatgcg
                                                                      240
geoogtggto etectaagtg tgagettgeg geggacegag gescacetge etecetgeet
gettegecca ggaetegtga etgegteege agaagaaate acaacagege tggaattget
agtttgctag gcagcatctt ttggacctgc gaaccatatg catttcacct caaatctgtt
tocaagttga aaacctttgg gtotttotat gogaacggat tgaagaaacg caaaaagttt
                                                                       420
ctacggactt taaattaaa atg gaa aaa tat gaa aac ctg ggt ttg gtt gga
                                                                      472
                     Met Glu Lys Tyr Glu Asr. Leu Gly Leu Val Gly
```

gaa ggg agt tat gga atg gtg atg aag tgt agg aat aaa gat act gga Glu Gly Ser Tyr Gly Met Val Met Lys Cys Arg Asn Lys Asp Thr Gly 15 20 25	520
aga att gtg gcc ata aag aag ttc tta gaa agt gac gat gac aaa atg Arg Ile Val Ala Ile Lys Lys Phe Leu Glu Ser Asp Asp Lys Met 30 35	568
gtt aaa aag att gca atg cga gaa gtc aag tta cta aag caa ctt agg Val Lys Lys Ile Ala Met Arg Glu Val Lys Leu Leu Lys Gln Leu Arg 45 50 55	616
cat gaa aac ttg gtg aat ctc ttg gaa gtg tgt aaa aaa aaa a His Glu Asn Leu Val Asn Leu Leu Glu Val Cys Lys Lys 60 65 70	659
<210> 127 <211> 301 <212> DN. <213> Homo sapiens	
<220> <221> CDS <222> 38283	
<221> sig_peptide <222> 3885 <223> Von Heijne matrix	
<221> polyA_signal <222> 257262	
<pre>&lt;400&gt; 127 cacctgaatc ccaggaaccc tcaatgaggt cttcaag atg aag aga ctg ctg cca</pre>	55
gct acc agc ctg gct ggc cct gtc ctg tcc acc ctc att gcc cca act Ala Thr Ser Leu Ala Gly Pro Val Leu Ser Thr Leu Ile Ala Pro Thr -10 -5 1 5	103
ccc atg ttg ttt tgt gaa gat aaa agc tgg gat ctt ttt ctt ttt Pro Met Leu Phe Cys Glu Asp Lys Ser Trp Asp Leu Phe Leu Phe Phe  10 20	151
aag tot cac aag aca tgg ggc atc too aca aat tta agt too tgt coa Lys Ser His Lys Thr Trp Gly Ile Ser Thr Asn Leu Ser Ser Cys Pro 25 30 35	199

ttt gga aat ttg ttt cta tgt gta cag ttt gtc aga gaa aaa caa agt Phe Gly Asn Leu Phe Leu Cys Val Gln Phe Val Arg Glu Lys Gln Ser

ttt tgt atg aat aca gaa tgt gat tta cgc aag aat tgacaaaaaa

293

301

45

60

Phe Cys Met Asn Thr Glu Cys Asp Leu Arg Lys Asn

<210> 128 <211> 477 <212> DNA

aaaaaaa

<213> Homo sapiens

<220>

<221> CDS <222> 121..477 <221> sig_peptide <222> 121..288 <223> Von Heijne matrix score 3.5 seq SSCADSFVSSSSS/QP <400> 128 cctcggagca ggcggagtaa agggacttga gcgagccagt tgccggatta ttctatttcc 60 cotcoctotc tocogcoccg tatetettt caccettete ceaccetege tegegtagee. 120 atg gcg gag ccg tcg gcg gcc act cag tcc cat tcc atc tcc tcg tcg Met Ala Glu Pro Ser Ala Ala Thr Gln Ser His Ser Ile Ser Ser Ser - 5,5. -50 tec tte gga gee gag eeg tee geg eee gge gge gge ggg age eea gga 216 Ser Phe Gly Ala Glu Pro Ser Ala Pro Gly Gly Gly Ser Pro Gly -35 -30 ged tige ded ged dtg ggg acg aag age tige age tied tied tigt geg gat 264 Ala Cys Pro Ala Leu Gly Thr Lys Ser Cys Ser Ser Ser Cys Ala Asp -20 -15 too tit git tot too tot too tot cag oot gia tot ota tit tog acc 312 Ser Phe Val Ser Ser Ser Ser Ser Gln Pro Val Ser Leu Phe Ser Thr - 5 tca caa gag gga ttg agc tct ctt tgc tct gat gag cca tct tca gaa Ser Gln Glu Gly Leu Ser Ser Leu Cys Ser Asp Glu Pro Ser Ser Glu 15 20 att atg act tot too ttt ott toa tot tot gaa ata oat aac act ggo 408 Ile Met Thr Ser Ser Phe Leu Ser Ser Ser Glu Ile His Asn Thr Gly 30 ctt aca ata cta cat gga gaa aaa agc cat gtg tta ggg agc cag cct 456 Leu Thr Ile Leu His Gly Glu Lys Ser His Val Leu Gly Ser Gln Pro 45 50 att tta gcc aaa aaa aaa aaa 477 Ile Leu Ala Lys Lys Lys Lys 60 <210> 129 <211> 323 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 2..163 <221> polyA signal <222> 292..297 <221> polyA site <222> 310..323 <400> 129 a gct ttc gtg tgg gag cca gct atg gtg cgg atc aat gcg ctg aca gca Ala Phe Val Trp Glu Pro Ala Met Val Arg Ile Asn Ala Leu Thr Ala ged tot gag got gog tgo etg atc gtg tot gta gat gaa acc atc aag 97 Ala Ser Glu Ala Ala Cys Leu Ile Val Ser Val Asp Glu Thr Ile Lys

25

aac dee ege tog act gtg gat get dee aca gea gea gge egg gge egt

145

20 .

WO 99/31236 -104- PCT/IB98/02122

	Pro	Arg 35	Ser	Thr	Val	Asp	Ala 40	Pro	Thr .	Ala		Gly 45	Arg	Gly	Arg	
	-		cgc Arg			tgag	aggc	ac c	ccac	ccat	c ac	atgg	ctgg			193
	ctgo	gc c													ggggt caaaa	253 313 323
	> 13 > DN	92 IA	apie	ns												
<220 <221 <222			5													
<222	> 46 > Vo sc	n He ore	ijne	mat		IV										
	-		sign 1369													
	-	-	site 1392													
<400 ctcc			caco	cago	g <b>a</b> aa	aaga	gggc	tcc	tctg	gga	gatg	t at Me	g ct	t ac	t ctc	57
ctcc	gagt ggc	tg o	caco tca Ser	ttc	atc	ttg	gca	gga	ctt	att	gtt	Me ggt	t Le gga	u Th gcc	r Leu tgc	57 105
tta Leu -10	gagt ggc Gly tac	ctt Leu aag	tca	ttc Phe ttc	atc Ile -5 atg	ttg Leu ccc	gca Ala aag	gga Gly agc	ctt Leu acc	att Ile 1 att	gtt Val tac	Me ggt Gly cgt	t Le gga Gly gga	u Th gcc Ala 5 gag	r Leu tgc Cys atg	
tta Leu -10 att Ile	gagt ggc Gly tac Tyr	ctt Leu aag Lys ttt Phe	tca Ser tac Tyr	ttc Phe ttc Phe	atc Ile -5 atg Met	ttg Leu ccc Pro	gca Ala aag Lys cct	gga Gly agc Ser 15 gca	ctt Leu acc Thr	att Ile 1 att Ile	gtt Val tac Tyr	ggt Gly cgt Arg	gga Gly gga Gly 20 gga	gcc Ala 5 gag Glu	tgc Cys atg Met	105
tta Leu -10 att Ile tgc Cys	ggc Gly tac Tyr ttt Phe aac Asn	ctt Leu aag Lys ttt Phe 25	tca Ser tac Tyr 10 gat	ttc Phe ttc Phe tct ser	atc Ile -5 atg Met gag Glu	ttg Leu ccc Pro gat Asp act Thr	gca Ala aag Lys cct Pro 30 gag	gga Gly agc Ser 15 gca Ala	ctt Leu acc Thr aat Asn	att Ile 1 att Ile tcc Ser	gtt Val tac Tyr ctt Leu	Meggt Gly cgt Arg cgt Arg 35 cgt	gga Gly gga Gly 20 gga Gly	gcc Ala 5 gag Glu gga Gly gat	tgc Cys atg Met gag Glu	105
tta Leu -10 att Ile tgc Cys cct Pro	gggc Gly tac Tyr ttt Phe aac Asn 40	ctt Leu aag Lys ttt Phe 25 ttc Phe	tca Ser tac Tyr 10 gat Asp	ttc Phe ttc Phe tct Ser cct Pro	atc Ile -5 atg Met gag Glu gtg Val gat Asp	ttg Leu ccc Pro gat Asp act Thr 45 gtg	gca Ala aag Lys cct Pro 30 gag Glu	gga Gly agc ser 15 gca Ala gag Glu	ctt Leu acc Thr aat Asn gct Ala	att Ile 1 att Ile tcc Ser gac Asp agt Ser	gtt Val tac Tyr ctt Leu att Ile 50	Meggt Gly cgt Arg cgt Arg Arg Arg Arg tct	gga Gly gga Gly 20 gga Gly gag Glu	gcc Ala 5 gag Glu gga Gly gat Asp	tgc Cys atg Met gag Glu gac Asp	105 153 201
tta Leu -10 att Ile tgc Cys cct Pro aac Asn 55	gagt ggc Gly tac Tyr ttt Phe aac Asn 40 att Ile	ctt Leu aag Lys ttt Phe 25 ttc Phe gca Ala	tca Ser tac Tyr 10 gat Asp ctg Leu	ttc Phe ttc Phe tct Ser cct Pro att Ile	atc Ile -5 atg Met gag Glu gtg Val gat Asp 60 cat	ttg Leu ccc Pro gat Asp act Thr 45 gtg Val	gca Ala aag Lys cct Pro 30 gag Glu cct Pro	gga Gly agc Ser 15 gca Ala gag Glu gtc Val	ctt Leu acc Thr aat Asn gct Ala ccc Pro aag Lys	att Ile 1 att Ile tcc Ser gac Asp agt Ser 65 gga	gtt Val tac Tyr ctt Leu att Ile 50 ttc Phe	ggt Gly cgt Arg cgt Arg 35 cgt Arg tct Ser	et Le gga Gly gga Gly 20 gga Gly gag Glu gat Asp	gcc Ala 5 gag Glu gga Gly gat Asp agt Ser tac Tyr	tgc Cys atg Met gag Glu gac Asp gac Asp	105 153 201 249
tta Leu -10 att Ile tgc Cys cct Pro aac Asn 55 cct Pro	ggc Gly tac Tyr ttt Phe aac Asn 40 att Ile gca Ala	ctt Leu aag Lys ttt Phe 25 ttc Phe gca Ala gca Ala	tca Ser tac Tyr 10 gat Asp ctg Leu atc Ile att Ile ctg Leu	ttc Phe ttc Phe tct Ser cct Pro att Ile att Ile 75	atc Ile -5 atg Met gag Glu gtg Val gat Asp 60 cat His	ttg Leu ccc Pro gat Asp act Thr 45 gtg Val gac Asp	gca Ala aag Lys cct Pro 30 gag Glu cct Pro ttt Phe	gga Gly agc Ser 15 gca Ala gag Glu gtc Val gaa Glu	ctt Leu acc Thr aat Asn gct Ala ccc Pro aag Lys 80 atg	att Ile 1 att Ile tcc Ser gac Asp agt Ser 65 gga Gly	gtt Val tac Tyr ctt Leu att Ile 50 ttc Phe atg Met	Meggt Gly cgt Arg cgt Arg 35 cgt Arg tct Ser act Thr	gga Gly gga Gly 20 gga Gly gag Glu gat Asp gct Ala	eu The geocean Ala 5 gag Glu gga Gly gat Asp agt tac Tyr 85 tct	tgc Cys atg Met gag Glu gac Asp gac Asp 70 ctg Leu	105 153 201 249 297
tta Leu -10 att Ile tgc Cys cct Pro aac Asn 55 cct Pro gac Asp	ggc Gly tac Tyr ttt Phe aac Asn 40 att Ile gca Ala ttg Leu atg	ctt Leu aag Lys ttt Phe 25 ttc Phe gca Ala gca Ala ttg Leu cct	tca Ser tac Tyr 10 gat Asp ctg Leu atc Ile att	ttc Phe ttc Phe tct Ser cct Pro att Ile att Ile 75 999 Gly	atc Ile -5 atg Met gag Glu gtg Val gat Asp 60 cat His atc Ile	ttg Leu ccc Pro gat Asp act Thr 45 gtg Val gac Asp tgc Cys	gca Ala aag Lys cct Pro 30 gag Glu cct Pro ttt Phe tat Tyr	gga Gly agc Ser 15 gca Ala gag Glu gtc Val gaa Glu ctg Leu 95 gag	ctt Leu acc Thr aat Asn gct Ala ccc Pro aag Lys 80 atg Met	att Ile 1 att Ile tcc Ser gac Asp agt Ser 65 gga Gly ccc Pro	gtt Val tac Tyr ctt Leu att Ile 50 ttc Phe atg Met ctc Leu	Meggt Gly cgt Arg cgt Arg 35 cgt Arg tct Ser act Thr aat Asn aaa	gga Gly gga Gly 20 gga Gly gag Glu gat Asp gct Ala act 100 ctg	eu The geocean Ala 5 gag Glu gga Gly gat Asp agt tac Tyr 85 tet Ser geg	teu tgc Cys atg Met gag Glu gac Asp gac Asp teu att Ile	105 153 201 249 297 345

WO 99/31236 -105- PCT/IB98/02122

gtg gag gaa att cgt gat gtt agt aac ctt ggc atc ttt att tac caa Val Glu Glu Ile Arg Asp Val Ser Asn Leu Gly Ile Phe Ile Tyr Gln 135 140 145 150	537
ctt tgc aat aac aga aag tcc ttc cgc ctt cgt cgc aga gac ctc ttg Leu Cys Asn Asn Arg Lys Ser Phe Arg Leu Arg Arg Arg Asp Leu Leu	585
ctg ggt ttc aac aaa cgt gcc att gat aaa tgc tgg aag att aga cac Leu Gly Phe Asn Lys Arg Ala Ile Asp Lys Cys Trp Lys Ile Arg His	633
170 175 180  ttc ccc aac gaa ttt att gtt gag acc aag atc tgt caa gag  Phe Pro Asn Glu Phe Ile Val Glu Thr Lys Ile Cys Gln Glu  185 190 195	675
taagaggcaa cagatagagt gtccttggta ataagaagtc agagatttac aatatgactt taacattaag gtttatggga tactcaagat atttactcat gcatttactc tattgcttat gctttaaaaa aaggaaaaaa aaaaaactac taaccactgc aagctcttgt caaaattttag tttaattggc attgcttgtt ttttgaaact gaaattacat gagtttcatt ttttcctttgc atttataggg tttagattc tggaaagcagc atgaatatat cacctaacat cctqacaata aattccatcc gttgttttt ttggttgtt gtttttctt tttaaaatt tttaaattgtt ttttgaacttt ttggtgtaaaa tatacagat cctcaacattg ttggtttctt ttggtgtaaaa tatacagat cctcaacattg ttggtttctt ttgttttca ttttttacacttgaacttattggaacattt catgagacag tcattttaa ggtgctctgt aattaacctg acttatatgt gaacaatttt catgagacag tcatttttaa ctaatgcagt gattctttttaagttggtat tgaattctac aaccctataa taaattttac tctatacaaa aaaaaaaa	735 795 855 915 975 1035 1095 1155 1215 1275 1335 1392
<210> 131 <211> 999 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 62385	
<221> polyA_signal <222> 974979	
<221> polyA_site <222> 987999	
<pre>&lt;400&gt; 131 cctgaatgac ttgaatgttt ccccgcctga gctaacagtc catgtgggtg attcagctct g atg gga tgt gtt ttc cag agc aca gaa gac aaa tgt ata ttc aag ata   Met Gly Cys Val Phe Gln Ser Thr Glu Asp Lys Cys Ile Phe Lys Ile 1 5 10 15</pre>	60 109
gac tgg act ctg tca cca gga gag cac gcc aag gac gaa tat gtg cta Asp Trp Thr Leu Ser Pro Gly Glu His Ala Lys Asp Glu Tyr Val Leu 20 25 30	157
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac.cgc Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg 35 40 45	205
gta cac ttg atg ggg gac atc tta tgc aat gat ggc tct ctc ctg ctc Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu Leu 50 55 60	253
caa gat gtg caa gag gct gac cag gga acc tat atc tgt gaa atc cgc Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg	301
ctc aaa ggg gag agc cag gtg ttc aag aag gcg gtg gta ctg cat gtg Leu Lys Gly Glu Ser Gln Val Phe Lys Lys Ala Val Val Leu His Val 85 90 95	349

ctt cca gag gag ccc aaa ggt acg caa atg ctt act taaagagggg Leu Pro Glu Glu Pro Lys Gly Thr Gln Met Leu Thr 100 105	395
ccaaggggca agagctttca tgtgcaagag gcaaggaaac tgattatctt gagtaaatgc cagctttgg gctaagtact taccacagag tgaatcttca aaaaatgatc ataattattt cagtcaataa aaatagagtt attttattaa ataaaatatt gataattatt gtattattac tttaaacaca cttcccctc acaaaagccc tgtgaaggat gttttgttca catatatgtc caaatatgtt ttggacacat atttattaaa tggaataaat agtacttgaa ccctggcacc tctgacaaca aagtccatgt tctttttact atgccctaat acctttcatc agttatccac attgatgcta catctgtatt ttataggtac cctatgttag gtgttctggg ggatagaaaa gaaataagca ggccaggctc agtggctcat gcctgtaatc ctagcatttt gggaggctga ggcagcagaa ctgcctgagc cccagggttc aagactgcag tgagctatga tggcaccact gcattctagc ctgggtgaca gagcaagact ctgtctaaaa taaaaaaaga gaaaaaaaaa aaaa	455 515 575 635 695 755 815 875 935 995
<210> 132 <211> 725 <212> DNA <213> Homo sapiens <220> <221> CDS	
<222> 422550  <221> sig_peptide <222> 422475  <223> Von Heijne matrix	
<221> polyA_site <222> 714725	
<pre>&lt;400&gt; 132 tctgcgaggg tgggagagaa aattaggggg agaaaggaca gagagagcaa ctaccatcca tagccagata ggtgagtaaa tatatttgca gtaacctatt tgctattcct tgctgcaact gtgtttaatg ttccttccag aatcagagag agtattgcca tccaagaaat cgtttttaga tatgacattt gagctatcat cttgagacca atacctaaaa caatttcagt ttaagaaatg tctaggtatg gtgaaaacac agtttaaaac cagcaaaaca gaatttattg ccctcagcga atacccacaa tgtacatata ccttgtattt ctgaaagcaa agcaagcatg ccaagtagtt tttatttacc tgtacctata atacagcaag gtgaaacagg atatattttt gaagtttaaa a atg tct tca ggc cgg ctg cgg tgg ctc atg cct gta atc cca gca ctt Met Ser Ser Gly Arg Leu Arg Trp Leu Met Pro Val Ile Pro Ala Leu -15</pre>	60 120 180 240 300 360 420 469
tgg gga gcc gag aag ggt gaa tca cct gag gtc agc agt ttt gag acc Trp Gly Ala Glu Lys Gly Glu Ser Pro Glu Val Ser Ser Phe Glu Thr	517
agg ctg gcc aac atg gcg aaa ccc tgt ctc tac tgaaaataca aaaattagct Arg Leu Ala Asn Met Ala Lys Pro Cys Leu Tyr 15 20 25	570
gggtgtggtg gegggegeet gtagteecag etaettggga gaetgaggea ggagaattge ttgaacaegg aaggeggaag ttgeagtaag etgagategt gecaeegeae accagettgg geaacagagt gagaeteect etcaaaaaaa aaaaa	630 690 725

<210> 133 <211> 400

<212> DNA

<213> Homo sapiens

WO 99/31236 -107- PCT/IB98/02122

<220> <221> CDS <222> 12423	1
<221> polyA_s <222> 38740	
<400> 133 ctcgcctctc ct	ggottotg gtatgcacca gcaattootg gogttoottg gotootagaa 60
gcatcactcc ta tgc atg tct g	tcacatgg tcatcttcac cctgtgtgtc ttcacactac cctttctctg 120 cc cga atc cct ttt tat aag gac acc agt cag att aga 168 la Arg Ile Pro Phe Tyr Lys Asp Thr Ser Gln Ile Arg 5 10 15
tta ggg tct a	cc ata ata cct cat ttt aac tta atc acc ttt gta aag 216 hr Ile Ile Pro His Phe Asn Leu Ile Thr Phe Val Lys 20 25 30
acc ttt ttc co Thr Phe Phe G	
	aggacaca attgaaccca taacagggtg tttgcaagga agagttaaaa 331 gtggtatt tgcttagata gatagggcac agctttctag gtgacaaaaa 391 400
<210> 134 <211> 1053 <212> DNA	
<213> Homo sap	piens
<220> <221> CDS	
<2225 CDS <222> 13110!	51
<221> sig_pep <222> 13116 <223> Von Hei score 4 seq MLA	jne matrix
<221> polyA_s: <222> 10191	
<400> 134	
	cgggctgc gacagcgccg gcccctgcgg ccgcaggtcg tcacagacga 60 cccggagg ctaaggacgg cagctccttt agcggcagag ttttccgagt 120
gaccttcttg at	g ctg gct gtt tct ctc acc gtt ccc ctg ctt gga gcc 165 t Leu Ala Val Ser Leu Thr Val Pro Leu Leu Gly Ala -10 -5
	tg gaa tot oot ata gat ooa cag oot oto ago tto aaa 21 eu Glu Ser Pro Ile Asp Pro Gln Pro Leu Ser Phe Lys 5 10 15
gaa ccc ccg c Glu Pro Pro L 2	to tig cit ggt git cig cat coa aat acg aag cig cga 26 eu Leu Leu Gly Val Leu His Pro Asn Thr Lys Leu Arg 0 25 30
Gln Ala Glu A 35	gg ctg ttt gaa aat caa ctt gtt gga ccg gag tcc ata 31 rg Leu Phe Glu Asn Gln Leu Val Gly Pro Glu Ser Ile 40 45
gca cat att g Ala His Ile G 50	gg gat gtg atg ttt act ggg aca gca gat ggc cgg gtc 36 ly Asp Val Met Phe Thr Gly Thr Ala Asp Gly Arg Val 55 60

	gta Val	aaa Lys	ctt Leu	gaa Glu	aat Asn	ggt Gly	gaa Glu	ata Ile	gag Glu	acc Thr	att Ile	gcc Ala	cgg Arg	ttt Phe	ggt Glv	tcg Ser		409
	65					70					75					80		
	ggc	cct	tgc	aaa	acc	cga	gat	gat	gag	cct	gtg	tgt	999	aga	CCC	ctg		457
	Gly	Pro	Cys	Lys	Thr 85	Arg	Asp	Asp	Glu	Pro 90	Val	Cys	Gly	Arg	Pro 95	Leu		
	ggt	atc	cgt	gca	999	CCC	aat	999	act	ctc	ttt	gtg	gcc	gat	gca	tqc		505
	Gly	Ile	Arg	Ala 100	Gly	Pro	Asn	Gly	Thr 105	Leu	Phe	Val	Āla	Asp 110	Āla	Cys		
	aag	gga	cta	ttt	gaa	gta	aat	ccc	tqq	aaa	cat	qaa	ata	aaa	cta	cta		553
	Lys	Gly	Leu	Phe	Glu	Val	Asn	Pro	Trp	Lvs	Ara	Glu	Val	Lva	Leu	Leu		
	-	•	115					120		-1-	5		125	-,-				
	ctg	tcc	tcc	gag	aca	ccc	att	gag	999	aag	aac	atg	tcc	ttt	gtg	aat		601
							Ile											
		130					135					140						
	gat	ctt	aca	gtc	tct	cag	gat	999	agg	aag	att	tat	ttc	acc	gat	tct		649
	Asp	Leu	Thr	Val	Ser	Gln	Asp	Gly	Arg	Lys	Ile	Tyr	Phe	Thr	Asp	Ser		
	145					150	_	=	-	•	155	•			•	160		
	aqc	agc	aaa	taa	caa	aga	cga	qac	tac	cta	ctt	cta	ata	atq	gag	aac	4	697
•	_	-				-	Arg	_		_		_		_				
			-1-		165				-1-	170					175	Q-7		
	aca	gat	gac	ggg	cqc	ctq	ctg	gag	tat	gat	act	ata	acc	agg	gaa	qta		745
							Leu											
		-	-	180	-				185	•			-	190		-		
	aaa	qtt	tta	ttq	qac	caq	ctg	caa	ttc	ccq	aat	gga	atc		ctq	tct		793
							Leu											
	-7 -		195					200				01,	205	<b></b>				
,	cct	gca	gaa	gac	ttt	gtc	ctg	gtg	gca	gaa	aca	acc	atg	qcc	agg	ata		841
							Leu											
		210					215					220			3			
1	cga	aga	gtc	tac	gtt	tct	ggc	ctg	atg	aag	ggc	<b>999</b>	gct	gat	ctg	ttt		889
							Gly											
	225	_		-		230	_			-	235	•		-		240		
	ata	gag	aac	atq	cct	gga	ttt	cca	gac	aac	atc	caa	ccc	aσc	agc	tct		937
				-			Phe		_					_	_			
					245	01,				250				002	255			
1	<b>999</b>	999	tac	tgg	gtg	ggc	atg	tcg	acc	atc	cgc	cct	aac	cct	ggg	ttt		985
							Met											
	•	-	•	260		•			265		_			270	•			
	tcc	atg	ctg	gat	ttc	tta	tct	gag	aga	ccc	tgg	att	aaa	agg	atg	att	1	033
							Ser											
			275	•				280	_		•		285					
	ttt	aag	gca	aaa	aaa	aaa	aa			•							1	053
					Lys													
		290		-	•	-												

<210> 135

<211> 1128

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 86..403

<221> sig_peptide <222> 86..181

<223> Von Heijne matrix score 8.8 seq VPMLLLIVGGSFG/LR

```
<221> polyA_signal
 <222> 1097..1102
 <221> polyA_site
 <222> 1117..1128
 <400> 135
 cgtcttggtg agagcgtgag ctgctgagat ttgggagtct gcgctaggcc cgcttggagt
 totgagooga tggaagagtt cacto atg ttt gca coo gcg gtg atg cgt gct
                                                                      112
                             Met Phe Ala Pro Ala Val Met Arg Ala
                                     -30
                                                         -25
 ttt ogc aag aac aag act oto ggo tat gga gto occ atg ttg ttg otg
                                                                      160
 Phe Arg Lys Asn Lys Thr Leu Gly Tyr Gly Val Pro Met Leu Leu Leu
             -20
                                 -15
 att gtt gga ggt tot tit ggt ott ogt gag tit tot caa ato oga tat
                                                                      208
 Ile Val Gly Gly Ser Phe Gly Leu Arg Glu Phe Ser Gln Ile Arg Tyr
 gat gct gtg aag agt aaa atg gat cct gag ctt gaa aaa aaa ctg aaa
                                                                      256
 Asp Ala Val Lys Ser Lys Met Asp Pro Glu Leu Glu Lys Lys Leu Lys
                    15
                                        20
 gag aat aaa ata tot tta gag tog gaa tat gag aaa ato aaa gac too
                                                                      304
Glu Asn Lys Ile Ser Leu Glu Ser Glu Tyr Glu Lys Ile Lys Asp Ser
                 30
                                     35
 aag ttt gat gac tgg aag aat att cga gga ccc agg cct tqq qaa gat
                                                                      352
Lys Phe Asp Asp Trp Lys Asn Ile Arg Gly Pro Arg Pro Trp Glu Asp
            45
                                50
                                                     55
 cet gae etc etc caa gga aga aat eca gaa age ett aag act aag aca
                                                                      400
 Pro Asp Leu Leu Gln Gly Arg Asn Pro Glu Ser Leu Lys Thr Lys Thr
                             65
 act tgactctgct gattcttttt tccnnntttt ttttttttta aataaaaata
                                                                      453
ctattaactg gacttcctaa tatatacttc tatcaagtgg aaaggaaatt ccaggcccat
                                                                      513
ggaaacttgg atatgggtaa tttgatgaca aataatcttc actaaaggtc atgtacaggt
                                                                      573
                                                                      633
ttttatactt cccagctatt ccatctgtgg atgaaagtaa caatgttggc cacgtatatt
 ttacacctcg aaataaaaaa tgtgaatact gctccaaaaa aaaaaaccag taccgtgtag
                                                                      693
tetetetegt ggettggatt tacactggge aacgtggttg gaatgtatet ggetcagaac
                                                                      753
tatgatatac caaacctggc taaaaaactt gaagaaatta aaaaggactt ggatgccaag
                                                                      813
aagaaacccc ctagtgcatg agactgcctc cagcactgcc ttcaggatat accgattcta
                                                                      873
ctgctcttga gggcctcgtt tactatctga accaaaagct tttgttttcg tctccagcct
                                                                      933
cagcacttct cttctttgct agaccctgtg ttttttgctt taaagcaagc aaaatggggc
                                                                      993
Cocaattiga gaactaccog acgittocaa catactoaco tottoccata atcocittoc
                                                                     1053
aactgcatgg gaggttctaa gactggaatt atggtgctag attagtaaac atgactttta
                                                                     1113
acgaaaaaa aaaaa
                                                                     1128
```

<210> 136

<211> 254

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 37..162

<221> sig_peptide

<222> 37..93

<223> Von Heijne matrix score 9.5 sex LMCLSLCTAFALS/KP

<222> 224229	
<221> polyA_site <222> 243254	
<pre>&lt;400&gt; 136 tgtgctgtgg gggctacgag gaaagatcta attatc atg gac ctg cga cag ttt</pre>	54
ctt atg tgc ctg tcc ctg tgc aca gcc ttt gcc ttg agc aaa ccc aca Leu Met Cys Leu Ser Leu Cys Thr Ala Phe Ala Leu Ser Lys Pro Thr -10 -5	102
gaa aag aag gac cgt gta cat cat gag cct cag ctc agt gac aag gtt Glu Lys Lys Asp Arg Val His His Glu Pro Gln Leu Ser Asp Lys Val 5 10	150
cac aat gat att tgatagaacc aattgttgta cataaaacag atctgcgcat His Asn Asp Ile 20	202
atatatatat gtataaaaaa taataaaata atggaagatg aaaaaaaa	254
<210> 137 <211> 886 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 31381	
<221> sig_peptide <222> 3190 <223> Von Heijne matrix score 5.4	
seq AFVIACVLSLIST/IY	
<pre>seq AFVIACVLSLIST/IY  &lt;221&gt; polyA_site &lt;222&gt; 875886</pre>	
<221> polyA_site <222> 875886  <400> 137 ggaggatggg cgagcagtct gaatggcaga atg gat aac cgt ttt gct aca gca Met Asp Asn Arg Phe Ala Thr Ala	54
<221> polyA_site <222> 875886  <400> 137 ggaggatggg cgagcagtct gaatggcaga atg gat aac cgt ttt gct aca gca	<b>54</b>
<221> polyA_site <222> 875886  <400> 137 ggaggatggg cgagcagtet gaatggcaga atg gat aac cgt ttt gct aca gca	
<pre>&lt;221&gt; polyA_site &lt;222&gt; 875886  &lt;400&gt; 137 ggaggatggg cgagcagtct gaatggcaga atg gat aac cgt ttt gct aca gca</pre>	102
<pre>&lt;221&gt; polyA_site &lt;222&gt; 875886  &lt;400&gt; 137 ggaggatggg cgagcagtet gaatggcaga atg gat aac cgt ttt gct aca gca</pre>	102
<pre>&lt;221&gt; polyA_site &lt;222&gt; 875886  &lt;400&gt; 137 ggaggatggg cgagcagtet gaatggcaga atg gat aac cgt ttt gct aca gca</pre>	102 150 198

WO 99/31236 -111- PCT/IB98/02122

					2.5										
70 tct gt Ser Va 85												taat	gatt	gc	391
ccaatt	acat	gtaag	gcago		gttg	gtto	tct	ctct		taaa	gaaa	ta a	atcg	tqtat	451
cttctc															511
ttggtt															571
tttact	cact	catta	aaaat	a ct	tttc	atta	ctc	taac	aca	tgtt	ataa	ag a	aata	gttgg	631
aaaagt															691
aatcaa															751
tgcccc agactg															811 871
gttaaa				. L Ly	jacyc	agag	ıccy	gray	gcc	aaya	aacc	Ly L	atta	cayaa	886
200daa															500
							*								
<210>	138														
<211>						••									
<212>															
<213>	: omo	варіє	ens												
<220>															
<221>	בחב														
<222>		79													
<221>	sig pe	eptic	ie												
<222>															
<223> 1	Von He	eijne	mat	rix											
:	score	3.5					•								
:	seq L	JFNFI	LILI	CILT/	'IW										
<400>															
													~ .~		E 7
ccctta		ggttr	nttat	c ta	ngga	atco	cnn	ınaag	act	9999				g Gln	57
ccctta	cca q	atg	tca	gaa	aag	gat	gag	tat	cag	ttt	Me caa	t Gl	u Ar -3 can	g Gln 5 nna	57 105
ccctta	cca q	atg Met	tca	gaa	aag	gat	gag Glu	tat	cag	ttt	Me caa	cat His	u Ar -3 can	g Gln 5 nna	
tca ag	g gtt g Val	atg Met -30	tca Ser	gaa Glu	aag Lys	gat Asp	gag Glu -25	tat Tyr	cag Gln	ttt Phe	Me caa Gln	cat His	u Ar -3 can Xaa	g Gln 5 nna Xaa	105
tca aggser Are	g gtt g Val	atg Met -30	tca Ser	gaa Glu gtc	aag Lys	gat Asp aat	gag Glu -25 ttt	tat Tyr ttg	cag Gln ctc	ttt Phe atc	Me caa Gln ctt	cat His -20 acc	u Ar -3 can Xaa	g Gln 5 nna Xaa ttg	
tca ag	g gtt g Val g gan a Xaa	atg Met -30	tca Ser	gaa Glu gtc	aag Lys	gat Asp aat Asn	gag Glu -25 ttt	tat Tyr ttg	cag Gln ctc	ttt Phe	Me caa Gln ctt Leu	cat His -20 acc	u Ar -3 can Xaa	g Gln 5 nna Xaa ttg	105
tca age Ser Are gcg gn Ala Xa	g gtt g Val g gan a Xaa -15	atg Met -30 ctg Leu	tca Ser ctt Leu	gaa Glu gtc Val	aag Lys ttc Phe	gat Asp aat Asn -10	gag Glu -25 ttt Phe	tat Tyr ttg Leu	cag Gln ctc Leu	ttt Phe atc Ile	Me caa Gln ctt Leu -5	cat His -20 acc Thr	-3 can Xaa att Ile	g Gln 5 nna Xaa ttg Leu	105
tca age Ser Are gcg gn Ala Xa	g gtt g Val g gan a Xaa -15 c tgg	atg Met -30 ctg Leu	tca Ser ctt Leu	gaa Glu gtc Val	aag Lys ttc Phe	gat Asp aat Asn -10 cat	gag Glu -25 ttt Phe	tat Tyr ttg Leu	cag Gln ctc Leu	ttt Phe atc Ile	Mecaa Gln ctt Leu -5 ttg	cat His -20 acc Thr	u Ar -3 can Xaa att Ile	g Gln 5 nna Xaa ttg Leu act	105
tca age Ser Are gcg gn Ala Xa	g gtt g Val g gan a Xaa -15 c tgg	atg Met -30 ctg Leu	tca Ser ctt Leu ttt	gaa Glu gtc Val aaa Lys	aag Lys ttc Phe aat	gat Asp aat Asn -10 cat His	gag Glu -25 ttt Phe cga Arg	tat Tyr ttg Leu ttc Phe	cag Gln ctc Leu cgc Arg	ttt Phe atc Ile ttc	Me caa Gln ctt Leu -5 ttg Leu	cat His -20 acc Thr	u Ar -3 can Xaa att Ile gaa Glu	g Gln 5 nna Xaa ttg Leu act	105
tca agg Ser Ard gcg gn Ala Xada at Thr Ill	g gtt g Val g gan a Xaa -15 c tgg	atg Met -30 ctg Leu tta Leu	tca Ser ctt Leu ttt	gaa Glu gtc Val aaa Lys 5	aag Lys ttc Phe aat Asn	gat Asp aat Asn -10 cat His	gag Glu -25 ttt Phe cga Arg	tat Tyr ttg Leu ttc Phe	cag Gln ctc Leu cgc Arg	ttt Phe atc Ile ttc Phe	Me caa Gln ctt Leu -5 ttg Leu	cat His -20 acc Thr cat	can Xaa att Ile gaa Glu	g Gln 5 nna Xaa ttg Leu act Thr	105
tca agg Ser Ard gcg gn Ala Xa aca at Thr II gga gg	g gtt g Val g gan a Xaa -15 c tgg e Trp	atg Met -30 ctg Leu tta Leu	tca Ser ctt Leu ttt Phe	gaa Glu gtc Val aaa Lys 5	aag Lys ttc Phe aat Asn	gat Asp aat Asn -10 cat His	gag Glu -25 ttt Phe cga Arg	tat Tyr ttg Leu ttc Phe	cag Gln ctc Leu cgc Arg 10 gga	ttt Phe atc Ile ttc Phe	Mecaa Gln ctt Leu -5 ttg Leu att	cat His -20 acc Thr cat His	can Xaa att Ile gaa Glu	g Gln 5 nna Xaa ttg Leu act Thr 15 tat	105 153 201
tca agg Ser Ard gcg gn Ala Xada at Thr Ill	g gtt g Val g gan a Xaa -15 c tgg e Trp	atg Met -30 ctg Leu tta Leu	tca Ser ctt Leu ttt Phe	gaa Glu gtc Val aaa Lys 5	aag Lys ttc Phe aat Asn	gat Asp aat Asn -10 cat His	gag Glu -25 ttt Phe cga Arg	tat Tyr ttg Leu ttc Phe	cag Gln ctc Leu cgc Arg 10 gga	ttt Phe atc Ile ttc Phe	Mecaa Gln ctt Leu -5 ttg Leu att	cat His -20 acc Thr cat His	can Xaa att Ile gaa Glu	g Gln 5 nna Xaa ttg Leu act Thr 15 tat	105 153 201
tca agg Ser Ard gcg gn Ala Xa aca at Thr II gga gg Gly Gl	ggtt Val gan a Xaa -15 c tgg e Trp a gca	atg Met -30 ctg Leu tta Leu atg Met	tca Ser ctt Leu ttt Phe gtg Val 20	gaa Glu gtc Val aaa Lys 5 tat Tyr	aag Lys ttc Phe aat Asn ggc Gly	gat Asp aat Asn -10 cat His ctt Leu	gag Glu -25 ttt Phe cga Arg ata Ile	tat Tyr ttg Leu ttc Phe atg Met 25	cag Gln ctc Leu cgc Arg 10 gga Gly	ttt Phe atc Ile ttc Phe cta Leu	Me Caa Gln Ctt Leu -5 ttg Leu att Ile	cat His -20 acc Thr cat His tca Ser	LU Ar -3 can Xaa att Ile gaa Glu cga Arg 30	g Gln nna Xaa ttg Leu act Thr 15 tat Tyr	105 153 201
tca agg Ser Ard gcg gn Ala Xa aca at Thr II gga gg	g gtt yal gan a Xaa -15 tgg e Trp	atg Met -30 ctg Leu tta Leu atg Met	tca Ser ctt Leu ttt Phe gtg Val 20 act	gaa Glu gtc Val aaa Lys 5 tat Tyr	aag Lys ttc Phe aat Asn ggc Gly	gat Asp aat Asn -10 cat His ctt Leu	gag Glu -25 ttt Phe cga Arg ata Ile	tat Tyr ttg Leu ttc Phe atg Met 25 gga	cag Gln ctc Leu cgc Arg 10 gga Gly	ttt Phe atc Ile ttc Phe cta Leu	Mecaa Gln ctt Leu -5 ttg Leu att Ile	cat His -20 acc Thr cat His tca Ser	can Xaa att Ile gaa Glu cga Arg 30 tgt	g Gln nna Xaa ttg Leu act Thr 15 tat Tyr	105 153 201 249
tca agg Ser Ard gcg gn Ala Xa aca at Thr II gga gg Gly Gl gct ac Ala Th	ggtt Val gan a Xaa -15 c tgg e Trp a gca y Ala a gca r Ala	atg Met -30 ctg Leu tta Leu atg Met cca Pro	tca Ser Ctt Leu ttt Phe gtg Val 20 act	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp	aag Lys ttc Phe aat Asn ggc Gly att	gat Asp aat Asn -10 cat His ctt Leu gaa Glu	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly	cag Gln ctc Leu cgc Arg 10 gga Gly act	ttt Phe atc Ile ttc Phe cta Leu gtc Val	Caa Gln Ctt Leu -5 ttg Leu att Ile tgt Cys	cat His -20 acc Thr cat His tca Ser gac Asp	can Xaa att Ile gaa Glu cga Arg 30 tgt Cys	g Gln nna Xaa  ttg Leu  act Thr 15 tat Tyr  gta Val	105 153 201 249
tca agg Ser Ard gcg gn Ala Xa aca at Thr II gga gg Gly Gl gct ac Ala Th	ggtt Val gan a Xaa -15 c tgg e Trp a gca y Ala a gca r Ala a act	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35	tca Ser ctt Leu ttt Phe gtg Val 20 act Thr	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp	aag Lys ttc Phe aat Asn ggc Gly att Ile	gat Asp aat Asn -10 cat His ctt Leu gaa Glu	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr	ttt Phe atc Ile ttc Phe cta Leu gtc Val	Me caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc	cat His -20 acc Thr cat His tca Ser gac Asp 45 act	u Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac	g Gln  nna  Xaa  ttg  Leu  act  Thr  15  tat  Tyr  gta  Val  caa	105 153 201 249
tca agg Ser Ard gcg gn Ala Xa aca at Thr II gga gg Gly Gl gct ac Ala Th	g gtt g Val gan a Xaa -15 c tgg e Trp a gca y Ala a gca r Ala a act u Thr	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35	tca Ser ctt Leu ttt Phe gtg Val 20 act Thr	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp	aag Lys ttc Phe aat Asn ggc Gly att Ile	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr	ttt Phe atc Ile ttc Phe cta Leu gtc Val	Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val	cat His -20 acc Thr cat His tca Ser gac Asp 45 act	u Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac	g Gln  nna  Xaa  ttg  Leu  act  Thr  15  tat  Tyr  gta  Val  caa	105 153 201 249 297
tca agg Ser Ard gcg gn Ala Xa aca at Thr II gga gg Gly Gl gct ac Ala Th aaa ct Lys Le	ggtt Val gan a Xaa -15 c tgg e Trp a gca y Ala a gca r Ala a act u Thr	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35 ttc	tca Ser ctt Leu ttt Phe gtg Val 20 act Thr agt	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp cca Pro	aag Lys ttc Phe aat Asn ggc Gly att Ile cca Pro	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act Thr	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg Leu	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly ctg	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr	ttt Phe atc Ile ttc Phe cta Leu gtc Val	Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val 60	cat His -20 acc Thr cat His tca Ser gac Asp 45 act Thr	u Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys	g Gln  nna  Xaa  ttg  Leu  act  Thr  15  tat  Tyr  gta  Val  caa  Gln	105 153 201 249 297
tca agg Ser Ard gcg gn Ala Xa aca at Thr II gga gg Gly Gl gct ac Ala Th aaa ct Lys Le	gtt Val gan a Xaa -15 c tggge Trp a gca y Ala a gca r Ala a act t Thr t gaa	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35 ttc Phe	tca Ser ctt Leu ttt Phe gtg Val 20 act Thr agt Ser aaa	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp cca Pro	aag Lys ttc Phe aat Asn ggc Gly att Ile cca Pro	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act Thr 55 aga	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg Leu	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly ctg Leu	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr	ttt Phe atc Ile ttc Phe cta Leu gtc Val aat Asn	Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val 60 cac	cat His -20 acc Thr cat His tca Ser gac Asp 45 act Thr	LU Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac Asp atc	g Gln nna Xaa  ttg Leu  act Thr 15 tat Tyr  gta Val  caa Gln aat	105 153 201 249 297
tca agg Ser Ard gcg gn Ala Xad aca att Thr II gga gg Gly Gl gct ac Ala Th aaa ct Lys Le gtt ta Val Ty	gtt Val gan a Xaa -15 c tggge Trp a gca y Ala a gca r Ala a act t Thr t gaa	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35 ttc Phe	tca Ser ctt Leu ttt Phe gtg Val 20 act Thr agt Ser aaa	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp cca Pro	aag Lys ttc Phe aat Asn ggc Gly att Ile cca Pro aaa Lys	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act Thr 55 aga	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg Leu	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly ctg Leu	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr	ttt Phe atc Ile ttc Phe cta Leu gtc Val aat Asn	Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val 60 cac	cat His -20 acc Thr cat His tca Ser gac Asp 45 act Thr	LU Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac Asp atc	g Gln nna Xaa  ttg Leu  act Thr 15 tat Tyr  gta Val  caa Gln aat	105 153 201 249 297
tca agg Ser Ard gcg gn Ala Xa aca at Thr II gga gg Gly Gl gct ac Ala Th aaa ct Lys Le gtt ta Val Ty 65	ggtt Val gan a Xaa -15 c tggge Trp a gca y Ala a gca r Ala a act t Thr t gaa r Glu	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35 ttc Phe tat Tyr	tca Ser ctt Leu ttt Phe gtg Val 20 act Thr agt Ser aaa Lys	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp cca Pro	aag Lys ttc Phe aat Asn ggc Gly att Ile cca Pro aaa Lys	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act Thr 55 aga Arg	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg Leu gaa Glu	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly ctg Leu ata Ile	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr yal	ttt Phe atc Ile ttc Phe cta Leu gtc Val aat Asn cag Gln	Me Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val 60 cac His	cat His -20 acc Thr cat His tca Ser gac Asp 45 act Thr aac	LU Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac Asp atc Ile	g Gln nna Xaa  ttg Leu  act Thr 15 tat Tyr  gta Val  caa Gln  aat Asn	105 153 201 249 297 345
tca agg Ser Ard gcg gn Ala Xal aca ath Thr III gga gg Gly Gl gct ac Ala Th aaa ct Lys Le gtt ta Val Ty 65 cct ca	gtt Val gan a Xaa -15 ctgge Trp a gca y Ala a gca r Ala a act t gaa r Clu t caa	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35 ttc Phe tat Tyr	tca Ser ctt Leu ttt Phe gtg Val 20 act Thr agt Ser aaa Lys	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp cca Pro tac Tyr	aag Lys ttc Phe aat Asn ggc Gly att Ile cca Pro aaa Lys 70 ata	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act Thr 55 aga Arg	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg Leu gaa Glu	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly ctg Leu ata Ile	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr gtt Val agt Ser atg	ttt Phe atc Ile ttc Phe cta Leu gtc Val aat Asn cag Gln	Me Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val 60 cac His ttt	cat His -20 acc Thr cat His tca Ser gac Asp 45 act Thr aac Asn gat	u Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac Asp atc Ile cca	g Gln  5  nna  Xaa  ttg  Leu  act Thr  15  tat Tyr  gta Val  caa Gln  aat Asn	105 153 201 249 297
tca agg Ser Ard gcg gn Ala Xal aca att Thr II gga gg Gly Gl gct ac Ala Th aaa ct Lys Le gtt ta Val Ty 65 cct ca Pro Hi	gtt Val gan a Xaa -15 ctgge Trp a gca y Ala a gca r Ala a act t gaa r Clu t caa	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35 ttc Phe tat Tyr	tca Ser ctt Leu ttt Phe gtg Val 20 act Thr agt Ser aaa Lys	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp cca Pro tac Tyr	aag Lys ttc Phe aat Asn ggc Gly att Ile cca Pro aaa Lys 70 ata	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act Thr 55 aga Arg	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg Leu gaa Glu	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly ctg Leu ata Ile	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr gtt Val agt Ser atgg	ttt Phe atc Ile ttc Phe cta Leu gtc Val aat Asn cag Gln	Me Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val 60 cac His ttt	cat His -20 acc Thr cat His tca Ser gac Asp 45 act Thr aac Asn gat	u Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac Asp atc Ile cca	g Gln nna Xaa  ttg Leu  act Thr 15 tat Tyr  gta Val  caa Gln  aat Asn  gaa Glu	105 153 201 249 297 345
tca agg Ser Ard gcg gn Ala Xal aca ath Thr II gga gg Gly Gl gct ac Ala Th aaa ct Lys Le gtt ta Val Ty 65 cct ca Pro Hi	ggtt Val gan a Xaa -15 c tggge Trp a gca y Ala a gca r Ala a act t ggan c Glu t caa s Gln	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35 ttc Phe tat Tyr	tca Ser ctt Leu ttt Phe gtg Val 20 act Thr agt Ser aaa Lys aat	gaa Glu gtc Val aaa Lys 5 tat Tyr gat Asp cca Pro tac Tyr gct Ala	aag Lys ttc Phe aat Asn ggc Gly att Ile cca Pro aaa Lys 70 ata Ile	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act Thr 55 aga Arg	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg Leu gaa Glu	tat Tyr ttg Leu ttc Phe atg Met 25 gga Gly ctg Leu ata Ile aag Lys	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr gttl Ser atg	ttt Phe atc Ile ttc Phe cta Leu gtc Val aat Asn cag Gln 75 aca Thr	Me Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val 60 cac His ttt Phe	cat His -20 acc Thr cat His tca Ser Gac Asp 45 act Thr acc Asp	u Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac Asp atc Ile cca Pro	g Gln  5  nna  Xaa  ttg  Leu  act Thr  15  tat Tyr  gta Val  caa Gln  aat Asn  gaa Glu 95	105 153 201 249 297 345 393
tca agg Ser Ard gcg gn Ala Xala Thr Ill gga ggg Gly Gl gct ac Ala Th aaa ct Lys Le gtt ta Val Ty 65 cct ca Pro Hi 80 atc tt	gtt Val gan a Xaa -15 ctgge Trp a gca y Ala a act tf Gan t Gan ctca cca cca cca cca cca cca cca cca cc	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35 ttc Phe tat Tyr gga Gly	tca Ser ctt Leu ttt Phe gtg Val 20 tThr agt aaa Lys aat Asn	gaa Glu gtc Val aaa Lys tat Tyr gat Asp cca Pro tac Tyr gct Ala 85	aag Lys ttc Phe aat Asn ggc Gly att Ile cca Pro aaa Lys 70 ata Ile	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act Thr 55 aga Arg ctt Leu	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg Leu gaa Glu gaa Glu	tat Tyr ttg Leu ttc Phe atg Met 25 aggly ctg Leu ata Ile aggly	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr gttl agt Ser atg Met 90 aca	ttt Phe atc Ile ttc Phe cta Leu gtc Val aat Asn cag Cln 75 aca Thr	Me Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val 60 cac His ttt Phe cat	cat His -20 acc Thr cat His tca Ser Gac Asp 45 act Thr acc Asn gat Asp	u Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac Asp atc Ile cca Pro gga	g Gln 5 nna Xaa  ttg Leu act Thr 15 tat Tyr gta Val caa Gln aat Asn gaa Glu 95 tat	105 153 201 249 297 345
tca agg Ser Ard gcg gn Ala Xal aca ath Thr II gga gg Gly Gl gct ac Ala Th aaa ct Lys Le gtt ta Val Ty 65 cct ca Pro Hi	gtt Val gan a Xaa -15 ctgge Trp a gca y Ala a act tf Gan t Gan ctca cca cca cca cca cca cca cca cca cc	atg Met -30 ctg Leu tta Leu atg Met cca Pro 35 ttc Phe tat Tyr gga Gly	tca Ser ctt Leu ttt Phe gtg Val 20 tThr agt aaa Lys aat Asn	gaa Glu gtc Val aaa Lys tat Tyr gat Asp cca Pro tac Tyr gct Ala 85	aag Lys ttc Phe aat Asn ggc Gly att Ile cca Pro aaa Lys 70 ata Ile	gat Asp aat Asn -10 cat His ctt Leu gaa Glu act Thr 55 aga Arg ctt Leu	gag Glu -25 ttt Phe cga Arg ata Ile agt Ser 40 ctg Leu gaa Glu gaa Glu	tat Tyr ttg Leu ttc Phe atg Met 25 aggly ctg Leu ata Ile aggly	cag Gln ctc Leu cgc Arg 10 gga Gly act Thr gttl agt Ser atg Met 90 aca	ttt Phe atc Ile ttc Phe cta Leu gtc Val aat Asn cag Cln 75 aca Thr	Me Caa Gln ctt Leu -5 ttg Leu att Ile tgt Cys gtc Val 60 cac His ttt Phe cat	cat His -20 acc Thr cat His tca Ser Gac Asp 45 act Thr acc Asn gat Asp	u Ar -3 can Xaa att Ile gaa Glu cga Arg 30 tgt Cys gac Asp atc Ile cca Pro gga	g Gln 5 nna Xaa  ttg Leu  act Thr 15 tat Tyr  gta Val  caa Gln  aat Asn  gaa Glu 95 tat Tyr	105 153 201 249 297 345 393

WO 99/31236 -112 - PCT/IB98/02122

agt cta aag aag aga cac ttt ttt caa aac tta gga tct att tta acg Ser Leu Lys Lys Arg His Phe Phe Gln Asn Leu Gly Ser Ile Leu Thr 115 120 125	537									
tat gcc ttc ttg gga act gcc atc tcc tgc atc gtc ata ggg Tyr Ala Phe Leu Gly Thr Ala Ile Ser Cys Ile Val Ile Gly 130 135 140	579									
taagtgacat teggagetea agttgeaggt ggetgtgggg tetgtgatet gtgtgaggga tetaacactt eeaggattet tgetggetgg gaaaattgte tttttttat taatacacat atttgtatgt tttttetgae ttaatteeae ggettetgae aaatacaagg etteaaatea aageaaacta gaggattget ggaettetee tgtgagttet ggaettetga ettagggaat gtggateaet tgeettgagt tatgtgaage geattgeatt	639 699 759 819 879 939 9059 1119 1179 1239									
<210> 139 <211> 471 <212> DNA <213> Homo sapiens										
<220> <221> CDS <222> 92469										
<221> sig_peptide <222> 92172 <223> Von Heijne matrix score 7.9 seq VVVLALGFLGCYG/AK										
<221> polyA_signal										
<221> polyA_site <222> 458471										
<pre>&lt;400&gt; 139 gcaagtgcag aagtcggtga cggtgggcat ctgggtgtca atcgatgggg catcctttct gaagatcttc gggccactgt cgtccagtgc c atg cag ttt gtc aac gtg ggc l</pre>										
tac ttc ctc atc gca gcc ggc gtt gtg gtc ctt gct ctt ggt ttc ctg  Tyr Phe Leu Ile Ala Ala Gly Val Val Leu Ala Leu Gly Phe Leu -20 -15 -10 -5	160									
ggc tgc tat ggt gct aag act gag agc atg tgt gcc ctc gtg acg ttc Gly Cys Tyr Gly Ala Lys Thr Glu Ser Met Cys Ala Leu Val Thr Phe 1 5 10	208									
tto tto ato oto oto oto ato tto att got gag gtt goa got got gtg  Phe Phe Ile Leu Leu Ile Phe Ile Ala Glu Val Ala Ala Val  15 20 25	256									
gtc gcc ctg gtg tac acc aca atg gct gag cac ttc ctg acg ttg ctg Val Ala Leu Val Tyr Thr Thr Met Ala Glu His Phe Leu Thr Leu Leu 30 35 40	304									
gta gtg cct gcc atc aag aaa gat tat ggt tcc cag gaa gac ttc act Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp Phe Thr 45 50 55 60	352									

WO 99/31236 -113- PCT/IB98/02122

caa gtg tgg aac acc acc atg aaa ggg ctc aag tgc cgt ggc ttc acc Gln Val Trp Asn Thr Thr Met Lys Gly Leu Lys Cys Arg Gly Phe Thr 65 70 75	400
aac tat acg gat ttt gag gac tca ccc tac ttc aaa atg cat aaa cct Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Met His Lys Pro 80 85 90	448
gtt aca atg aaa aaa aaa aa Val Thr Met Lys Lys Lys 95	471
<210> 140 <211> 849 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 154675	
<221> sig_peptide <222> 154498 <223> Von Heijne matrix score 4.8 seq PLRLLNLLILIEG/GV	
<221> polyA_signal <222> 819824	
<221> polyA_site	
<222> 838849	
<400> 140 cccctatete cagaceteat tegeaatgaa gtagaatgte tgaaageaga ttteaaceae agaateaagg aggttetett caacteeete tteagtgeet actatgttge attteteeee etgtgttttg tgaagagtae ceagtaetat gae atg ege tgg tea tgt gag eae	60 120 174
<pre>&lt;400&gt; 140 cccctatctc cagacctcat tcgcaatgaa gtagaatgtc tgaaagcaga tttcaaccac agaatcaagg aggttctctt caactcctc ttcagtgcct actatgttgc atttctcccc ctgtgttttg tgaagagtac ccagtactat gac atg cgc tgg tca tgt gag cac</pre>	120 174
<pre>&lt;400&gt; 140 cccctatctc cagacctcat tcgcaatgaa gtagaatgtc tgaaagcaga tttcaaccac agaatcaagg aggttctctt caactcctc ttcagtgcct actatgttgc atttctcccc ctgtgttttg tgaagagtac ccagtactat gac atg cgc tgg tca tgt gag cac</pre>	120
<pre>&lt;400&gt; 140 cccctatctc cagacctcat tcgcaatgaa gtagaatgtc tgaaagcaga tttcaaccac agaatcaagg aggttctctt caactccctc ttcagtgcct actatgttgc atttctcccc ctgtgttttg tgaagagtac ccagtactat gac atg cgc tgg tca tgt gag cac</pre>	120 174
<pre>&lt;400&gt; 140 cccctatctc cagacctcat tcgcaatgaa gtagaatgtc tgaaagcaga tttcaaccac agaatcaagg aggttctctt caactcctc ttcagtgcct actatgttgc atttctcccc ctgtgttttg tgaagagtac ccagtactat gac atg cgc tgg tca tgt gag cac</pre>	120 174 222
<pre>&lt;400&gt; 140 cccctatctc cagacctcat tcgcaatgaa gtagaatgtc tgaaagcaga tttcaaccac agaatcaagg aggttctctt caactcctc ttcagtgcct actatgttgc atttctcccc ctgtgttttg tgaagagtac ccagtactat gac atg cgc tgg tca tgt gag cac</pre>	120 174 222 270
cccctatctc cagacctcat tcgcaatgaa gtagaatgtc tgaaagcaga tttcaaccac agaatcaagg aggttctctt caactccctc ttcagtgcct actatgttgc atttctcccc ctgtgttttg tgaagagtac ccagtactat gac atg cgc tgg tca tgt gag cac Met Arg Trp Ser Cys Glu His -115 -110  ctc gtt atg gtg tgg atc aat gct ttt gtc atg ctc acc acg caa ctg Leu Val Met Val Trp Ile Asn Ala Phe Val Met Leu Thr Thr Gln Leu -105 -100 -95  ttg cca tcc aaa tac tgt gat ttg cta cat aaa tca gct gct cac ctg Leu Pro Ser Lys Tyr Cys Asp Leu Leu His Lys Ser Ala Ala His Leu -90 -85 -80  ggc aag tgg cag aag ttg gaa cat ggg tcc tac agc aat gct cca cag Gly Lys Trp Gln Lys Leu Glu His Gly Ser Tyr Ser Asn Ala Pro Gln -75 -70 -65  cac att tgg tca gaa aat aca ata tgg cct caa ggg gtg ctg gtg cgg His Ile Trp Ser Glu Asn Thr Ile Trp Pro Gln Gly Val Leu Val Arg -60 -55 -50 -45  cac agc aga tgt tta tat aga gcc atg ggg cct tac aac gtg gca gtg His Ser Arg Cys Leu Tyr Arg Ala Met Gly Pro Tyr Asn Val Ala Val	120 174 222 270
cecetatete cagaceteat tegeaatgaa gtagaatgte tgaaageaga ttteaaceae agaateaagg aggttetett caacteete tteagtgeet actatgttge attteteee etgtgttttg tgaaagagtae ceagtactat gae atg ege tgg tea tgt gag cae Met Arg Trp Ser Cys Glu His -115 -110  cte gtt atg gtg tgg ate aat get ttt gte atg etc ace ace cae cae ctg Leu Val Met Val Trp Ile Asn Ala Phe Val Met Leu Thr Thr Gln Leu -105 -100 -95  ttg cca tee aaa tae tgt gat ttg eta cat aaa tea get get eac etg Leu Pro Ser Lys Tyr Cys Asp Leu Leu His Lys Ser Ala Ala His Leu -90 -85 -80  gge aag tgg cag aag ttg gaa cat ggg tee tae age aat get eea eag Gly Lys Trp Gln Lys Leu Glu His Gly Ser Tyr Ser Asn Ala Pro Gln -75 -70 -65  cae att tgg tea gaa aat ace at ace ata tgg etc ea ggg gtg etg gtg egg His Ile Trp Ser Glu Asn Thr Ile Trp Pro Gln Gly Val Leu Val Arg -60 -55 -50 -45  cae age aga tgt tta tat aga gee atg ggg ect tae aac gtg gea gtg His Ser Arg Cys Leu Tyr Arg Ala Met Gly Pro Tyr Asn Val Ala Val -40 -35 -30  cet tea gat gta tet cat gee ege ttt tat tte tta ttt cat ega eea Pro Ser Asp Val Ser His Ala Arg Phe Tyr Phe Leu Phe His Arg Pro	120 174 222 270 318
<pre>&lt;400&gt; 140 cccctatctc cagacctcat tcgcaatgaa gtagaatgtc tgaaagcaga tttcaaccac agaatcaagg aggttctctt caactccctc ctgtgttttg tgaaagagtac ccagtactat gac atg cgc tgg tca tgt gag cac</pre>	120 174 222 270 318 366

WO 99/31236 -114 - PCT/IB98/02122

5					10					15					20	
tcc	atg	gct	ctc	atc	ctc	ttc	tgc	aac	tac	tat	gtt	tta	ttt	aaa	ctt	606
Ser	Met	Ala	Leu	Ile	Leu	Phe	Cys	Asn	Tyr	Tyr	Val	Leu	Phe	Lys	Leu	
				25					30					35		
ctc	cgg	gac	aga	ata	gta	tta	ggc	agg	gca	tac	tcc	tac	cca	ctc	aac	654
Leu	Arg	Asp	Arg	Ile	Val	Leu	Gly	Arg	Ala	Tyr	Ser	Tyr	Pro	Leu	Asn	
			40					45					50			
agt	tat	gaa	ctc	aag	gca	aac	taag	gctg	ct o	ctcaa	acaat	g ag	ggag	gaact	t	705
Ser	Tyr	Glu	Leu	Lys	Ala	Asn										
		55											,			
caga	ataaa	aaa t	atti	tca	ca co	gttct	catit	ttt	tctt	gtg	att	ttat	taa a	atati	ttaaga	765
tgttttatat tttgtatact attatgtttt gaaagtcggg aagagtaagg gatattaaat								825								
gtatccgtaa acaaaaaaaa aaaa								849								

<210> 141 <211> 155 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -31..-1

<400> 141

Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser -25 -20 Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu -15 -10 - 5 Leu Leu Pro His Cys Gln Lys Pro Phe Val Tyr Asp Leu His Ala Val 10 Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys 25 30 Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe 40 4.5 Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu 55 60 Leu Gly Thr Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu 75 Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser 90 85 Gly Leu Ile Phe Cys Cys Ala Phe Cys Ser Glu Thr Lys Leu Phe Leu 105 100

Ser Arg Gln Ala Met Ala Glu Asn Phe Ser Ile

120

<210> 142 <211> 55 <212> PRT <213> Homo sapiens

115

-115-

50

55

```
<210> 143
<211> 67
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 143
Met Ser Arg Asn Leu Arg Thr Ala Leu Ile Phe Gly Gly Phe Ile Ser
                   -15
                                        -10
Leu Ile Gly Ala Ala Phe Tyr Pro Ile Tyr Phe Arg Pro Leu Met Arg
Leu Glu Glu Tyr Lys Lys Glu Gln Ala Ile Asn Arg Ala Gly Ile Val
                           20
Gln Glu Asp Val Gln Pro Pro Gly Leu Lys Val Trp Ser Asp Pro Phe
  30
                       35
Gly Arg Lys
45
```

<210> 144 <211> 198 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

## <400> 144

Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala Leu Ala Met Val Thr -15 Arg Pro Ala Ser Ala Ala Pro Met Gly Gly Pro Glu Leu Ala Gln His Glu Glu Leu Thr Leu Leu Phe His Gly Thr Leu Gln Leu Gly Gln Ala 20 Leu Asn Gly Val Tyr Arg Thr Thr Glu Gly Trp Leu Thr Lys Ala Arg 35 Asn Ser Leu Gly Leu Tyr Gly Arg Thr Ile Glu Leu Leu Gly Gln Glu 50 Val Ser Arg Gly Arg Asp Ala Ala Gln Glu Leu Arg Ala Ser Leu Leu Glu Thr Gln Met Glu Glu Asp Ile Leu Gln Leu Gln Ala Glu Ala Thr 85 Ala Glu Val Leu Gly Glu Val Ala Gln Ala Gln Lys Val Leu Arg Asp 100 Ser Val Gln Arg Leu Glu Val Gln Leu Arg Ser Ala Trp Leu Gly Pro 115 Ala Tyr Arg Glu Phe Glu Val Leu Lys Ala His Ala Asp Lys Gln Ser 130 135 His Ile Leu Trp Ala Leu Thr Gly His Val Gln Arg Gln Arg Glu 145 150 Met Val Ala Gln Gln His Arg Leu Arg Gln Ile Gln Glu Arg Leu His 165 Thr Ala Ala Leu Pro Ala

175

<210> 145 <211> 135 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -25..-1 <400> 145 Met Ser Leu Arg Asn Leu Trp Arg Asp Tyr Lys Val Leu Val Val Met -20 -15 Val Pro Leu Val Gly Leu Ile His Leu Gly Trp Tyr Arg Ile Lys Ser - 5 1 Ser Pro Val Phe Gln Ile Pro Lys Asn Asp Asp Ile Pro Glu Gln Asp 10 15 Ser Leu Gly Leu Ser Asn Leu Gln Lys Ser Gln Ile Gln Gly Lys Xaa 30 Ala Gly Leu Gln Ser Ser Gly Lys Glu Ala Ala Leu Asn Leu Ser Phe 45 40 50 Ile Ser Lys Glu Glu Met Lys Asn Thr Ser Trp Ile Arg Lys Asn Trp 65 Leu Leu Val Ala Gly Ile Ser Phe Ile Gly Asp His Leu Gly Thr Tyr 80 75 Phe Leu Gln Arg Ser Ala Lys Gln Ser Val Lys Phe Gln Ser Gln Ser 90 Lys Gln Lys Ser Ile Glu Glu 105

<210> 146 <211> 255 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -70..-1

<400> 146 Met Gln Gln Lys Glu Gln Gln Phe Arg Glu Trp Phe Leu Lys Glu Phe -60 -65 Pro Gln Ile Arg Trp Lys Ile Gln Glu Ser Ile Glu Arg Leu Arg Val -50 - 45 Ile Ala Asn Glu Ile Glu Lys Val His Arg Gly Cys Val Ile Ala Asn -30 -35 Val Val Ser Gly Ser Thr Gly Ile Leu Ser Val Ile Gly Val Met Leu -15 -10 Ala Pro Phe Thr Ala Gly Leu Ser Leu Ser Ile Thr Ala Ala Gly Val 1 Gly Leu Gly Ile Ala Ser Ala Thr Ala Gly Ile Ala Ser Ser Ile Val 20 15 Glu Asn Thr Tyr Thr Arg Ser Ala Glu Leu Thr Ala Ser Arg Leu Thr 35 30 Ala Thr Ser Thr Asp Gln Leu Glu Ala Leu Arg Asp Ile Leu His Asp 50 Ile Thr Pro Asn Val Leu Ser Phe Ala Leu Asp Phe Asp Glu Ala Thr WO 99/31236 -117- PCT/IB98/02122

65 Lys Met Ile Ala Asn Asp Val His Thr Leu Arg Arg Ser Lys Ala Thr 80 Val Gly Arg Pro Leu Ile Ala Trp Arg Tyr Val Pro Ile Asn Val Val 100 Glu Thr Leu Arg Thr Arg Gly Ala Pro Thr Arg Ile Val Arg Lys Val 115 Ala Arg Asn Leu Gly Lys Ala Thr Ser Gly Val Leu Val Val Leu Asp 125 130 Val Val Asn Leu Val Gln Asp Ser Leu Asp Leu His Lys Gly Glu Lys 145 150 Ser Glu Ser Ala Glu Leu Leu Arg Gln Trp Ala Gln Glu Leu Glu Glu 165 160 Asn Leu Asn Glu Leu Thr His Ile His Gln Ser Leu Lys Ala Gly 175 180

<210> 147 <211> 59 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -49..-1

<400> 147

Met Pro Gly Thr Glu Val Leu Glu Gly Ala Thr Asp Gly Leu Ala Ala
-45 - -40 -35

Ile Asn Leu Leu Lys Trp Ile Lys Thr Leu Gly Gly Ser Val Ile Ser
-30 -25 -20

Met Ile Val Leu Leu Ile Cys Val Val Cys Leu Tyr Ile Val Cys Arg
-15 -10 -5

Cys Gly Ser His Leu Trp Arg Glu Ser His His
1 10

<210> 148 <211> 180 <212> PRT <213> Homo sapiens

 <400> 148

 Met Cys Ile Ser Gly Leu Cys Gln Ile Val Gly Cys Asp His Gln Leu 1
 5
 10
 15

 Gly Ser Thr Val Lys Glu Asp Asn Cys Gly Val Cys Asn Gly Asp Gly 20
 25
 30

 Ser Thr Cys Arg Leu Val Arg Gly Gln Tyr Lys Ser Gln Leu Ser Ala 35
 40
 45

 Thr Lys Ser Asp Asp Thr Val Val Ala Ile Pro Tyr Gly Ser Arg His 50
 55
 60

 Ile Arg Leu Val Leu Lys Gly Pro Asp His Leu Tyr Leu Glu Thr Lys 65
 70
 75

 Thr Leu Gln Gly Thr Lys Gly Glu Asn Ser Leu Ser Ser Thr Gly Thr 85
 90
 95

 Phe Leu Val Asp Asn Ser Ser Val Asp Phe Gln Lys Phe Pro Asp Lys 100
 105
 110

 Glu Ile Leu Arg Met Ala Gly Pro Leu Thr Ala Asp Phe Ile Val Lys 125
 125

 Ile Arg Asn Ser Gly Ser Ala Asp Ser Thr Val Gln Phe Ile Phe Tyr

```
130

Gln Pro Ile Ile His Arg Trp Arg Glu Thr Asp Phe Phe Pro Cys Ser
145

150

160

Ala Thr Cys Gly Gly Gly Tyr Gln Leu Thr Ser Ala Glu Cys Tyr Asp
165

170

Leu Arg Ser Asn
180
```

<210> 149 <211> 162 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -23...1

<400> 149 Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala -15 -20 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu - 5 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe 20 15 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val 35 30 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu 50 55 45 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr 65 Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe 85 80 Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Pro Asp Asn 95 100 Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr 115 110 Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Val Ser Met

<210> 150 <211> 120 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -23..-1

Val Phe

<210> 151 <211> 7 <212> PRT <213> Homo sapiens <400> 151 Met Val Glu Met Thr Gly Val

<210> 152 <211> 199 <212> PRT <213> Homo sapiens ·

<220>
<221> SIGNAL
<222> -42..-1

<400> 152 Met Asp Gly Gln Lys Lys Asn Trp Lys Asp Lys Val Val Asp Leu Leu -35 Tyr Trp Arg Asp Ile Lys Lys Thr Gly Val Val Phe Gly Ala Ser Leu -15 -20 Phe Leu Leu Ser Leu Thr Val Phe Ser Ile Val Ser Val Thr Ala -5 Tyr Ile Ala Leu Ala Leu Leu Ser Val Thr Ile Ser Phe Arg Ile Tyr 10 15 Lys Gly Val Ile Gln Ala Ile Gln Lys Ser Asp Glu Gly His Pro Phe 35 30 Arg Ala Tyr Leu Glu Ser Glu Val Ala Ile Ser Glu Glu Leu Val Gln 50 45 Lys Tyr Ser Asn Ser Ala Leu Gly His Val Asn Cys Thr Ile Lys Glu 65 60 Leu Arg Arg Leu Phe Leu Val Asp Asp Leu Val Asp Ser Leu Lys Phe 80 Ala Val Leu Met Trp Val Phe Thr Tyr Val Gly Ala Leu Phe Asn Gly 95 Leu Thr Leu Leu Ile Leu Ala Leu Ile Ser Leu Phe Ser Val Pro Val 110 105 Ile Tyr Glu Arg His Gln Ala Gln Ile Asp His Tyr Leu Val Leu Ala 130 125 120 Asn Lys Asn Val Lys Asp Ala Met Ala Lys Ile Gln Ala Lys Ile Pro 145 140 Gly Leu Lys Arg Lys Ala Glu 155

```
<211> 43
<212> PRT
<213> Homo sapiens
<400> 153
Met Pro Phe Arg Met Ser Gly Tyr Ile Pro Phe Gly Thr Pro Ile Val
Ser Val Thr Phe Lys Gly Phe Pro Phe Leu Lys Asn Tyr Phe Lys Cys
           20
                               25
Leu Thr Leu Cys Tyr Cys Ser Arg Val Phe Asp
<210> 154
<211> 50
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
<400> 154
Met Glu Trp Ala Gly Lys Gln Arg Asp Phe Gln Val Arg Ala Ala Pro
                            -30
Gly Trp Asp His Leu Ala Ser Phe Pro Gly Pro Ser Leu Arg Leu Phe
                                        -10
   -20
                - -15
Ser Gly Ser Gln Ala Ser Val Cys Ser Leu Cys Ser Gly Phe Gly Ala
- 5
                . 1
Gln Glu
<210> 155
<211> 153
<212> PRT
<213> Homo sapiens
<400> 155
Thr Val Pro Leu Leu Glu Pro Ala Asp His Ala Arg Gly Arg Ala
                                    10
His Val His Leu Pro Glu Asn Val Arg Ser Gln Ser Pro Gly His Val
                                25
Arg Arg Gly Arg Ser Gly Ala Gln Val Leu Pro Thr Gly Pro Asp Glu
                                               45
                            40
Lys Gln Val Glu Lys Ser Glu Val Asp Phe Ser Lys Ser His Ser Leu
                        55
Val Arg Arg Phe Glu Asp Leu Lys Pro Lys Leu Ser Val Cys Lys Thr
Gly Ser Gln Val Phe Arg Ser Glu Asn Trp Lys Val Trp Ala Glu Ser
                                    90
Ser Arg Gly Asp His Asp Asp Cys Leu Asp Leu Cys Ser Val Leu Cys
                               105
            100
Trp Gly Glu Leu Leu Arg Thr Ile Pro Glu Ile Pro Pro Lys Arg Gly
                                               125
                           120
Glu Leu Lys Thr Glu Leu Leu Gly Leu Lys Glu Arg Lys His Lys Pro
                       135
Gln Val Ser Gln Gln Glu Glu Leu Lys
```

```
<210> 156
<211> 67
<212> PRT
<213> Homo sapiens
<400> 156
Met Arg Gln Lys Arg Lys Gly Asp Leu Ser Pro Ala Lys Leu Met Met
                                    10
Leu Thr Ile Gly Asp Val Ile Lys Gln Leu Ile Glu Ala His Glu Gln
          20
                               25
Gly Lys Asp Ile Asp Leu Asn Lys Val Arg Thr Lys Thr Ala Ala Lys
                           40
Tyr Gly Leu Ser Ala Gln Pro Arg Leu Val Asp Ile Ile Ala Ala Val
                       55
Pro Pro Glu
65
<210> 157
<211> 87
<212> PRT
<213> Homo sapiens
Met Asp Glu Leu Ser Glu Glu Asp Lys Leu Thr Val Ser Arg Ala Arg
                                    10
Lys Ile Gln Arg Phe Leu Ser Gln Pro Phe Gln Val Ala Glu Val Phe
                                25
Thr Gly His Met Gly Lys Leu Val Pro Leu Lys Glu Thr Ile Lys Gly
                            40
Phe Gln Gln Ile Leu Ala Gly Glu Tyr Asp His Leu Pro Glu Gln Ala
                        55
Phe Tyr Met Val Gly Pro Ile Glu Glu Ala Val Ala Lys Ala Asp Lys
                    70
Leu Ala Glu Glu His Ser Ser
                85
<210> 158
<211> 250
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -85..-1
<400> 158
Met Ser Ala Glu Val Lys Val Thr Gly Gln Asn Gln Glu Gln Phe Leu
                                         - 75
Leu Leu Ala Lys Ser Ala Lys Gly Ala Ala Leu Ala Thr Leu Ile His
                                     -60
Gln Val Leu Glu Ala Pro Gly Val Tyr Val Phe Gly Glu Leu Leu Asp
                                                     -40
                                -45
            -50
Met Pro Asn Val Arg Glu Leu Xaa Ala Arg Asn Leu Pro Pro Leu Thr
                                                 - 25
                            -30
        -35
Glu Ala Gln Lys Asn Lys Leu Arg His Leu Ser Val Val Thr Leu Ala
```

-15

Ala Lys Val Lys Cys Ile Pro Tyr Ala Val Leu Leu Glu Ala Leu Ala

- : 0

Leu Arg Asn Val Arg Gln Leu Glu Asp Leu Val Ile Glu Ala Val Tyr 20 Ala Asp Val Leu Arg Gly Ser Leu Asp Gln Arg Asn Gln Arg Leu Glu Val Asp Tyr Ser Ile Gly Arg Asp Ile Gln Arg Gln Asp Leu Ser Ala 50 Ile Ala Arg Thr Leu Gln Glu Trp Cys Val Gly Cys Glu Val Val Leu 65 70 Ser Gly Ile Glu Glu Gln Val Ser Arg Ala Asn Gln His Lys Glu Gln 80 85 Gln Leu Gly Leu Lys Gln Gln Ile Glu Ser Glu Val Ala Asn Leu Lys 100 Lys Thr Ile Lys Val Thr Thr Ala Ala Ala Ala Ala Thr Ser Gin 115 120 Asp Pro Glu Gln His Leu Thr Glu Leu Arg Glu Pro Ala Pro Gly Thr 130 135 Asn Gln Arg Gln Pro Ser Lys Lys Ala Ser Lys Gly Lys Gly Leu Arg 150 145 Gly Ser Ala Lys Ile Trp Ser Lys Ser Asn

<210> 159 <211> 24 <212> PRT <213> Homo sapiens

<210> 160 <211> 228 <212> PRT <213> Homo sapiens

Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr Thr Tyr Asn Lys His Ile Asn Ile Ser Phe His Arg Phe Pro Leu Asp Pro Lys Arg Arg 25 Lys Glu Trp Val Arg Leu Val Arg Arg Lys Asn Phe Val Pro Gly Lys His Thr Phe Leu Cys Ser Lys His Phe Glu Ala Ser Cys Phe Asp Leu Thr Gly Gln Thr Arg Arg Leu Lys Met Asp Ala Val Pro Thr Ile Phe 75 Asp Phe Cys Thr His Ile Lys Ser Met Lys Leu Lys Ser Arg Asn Leu 90 85 Leu Lys Lys Asn Asn Ser Cys Ser Pro Ala Gly Pro Ser Ser Leu Lys 105 100 Ser Asn Ile Ser Ser Gln Gln Val Leu Leu Glu His Ser Tyr Ala Phe 120 125 Arg Asn Pro Met Glu Ala Lys Lys Arg Ile Ile Lys Leu Glu Lys Glu 135 Ile Ala Ser Leu Arg Arg Lys Met Lys Thr Cys Leu Gln Lys Glu Arg

155 150 145 Arg Ala Thr Arg Arg Trp Ile Lys Ala Met Cys Leu Val Lys Asn Leu 170 175 165 Glu Ala Asn Ser Val Leu Pro Lys Gly Thr Ser Glu His Met Leu Pro 180 185 190 Thr Ala Leu Ser Ser Leu Pro Leu Glu Asp Phe Lys Ile Leu Glu Gln 195 200 205 Asp Gln Gln Asp Lys Thr Leu Leu Ser Leu Asn Leu Lys Gln Thr Lys 210 215 220 Ser Thr Phe Ile 225

<210> 161
<211> 86
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1

<400> 161 Met Asn Leu His Phe Pro Gln Trp Phe Val His Ser Ser Ala Leu Gly -15 -10 Leu Val Leu Ala Pro Pro Phe Ser Ser Pro Gly Thr Asp Pro Thr Phe 10 1 5 Pro Cys Ile Tyr Cys Arg Leu Leu Asn Met Ile Met Thr Arg Leu Ala 20 15 Phe Ser Phe Ile Thr Cys Leu Cys Pro Asn Leu Lys Glu Val Cys Leu 40 35 Ile Leu Pro Glu Lys Asn Cys Asn Ser Arg His Ala Gly Phe Val Gly 45 50 Pro Ala Lys Leu Arg Gln

<210> 162 <211> 44 <212> PRT <213> Homo sapiens

<210> 163 <211> 314 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -58..-1

```
<400> 163
Met Gln Asn Val Ile Asn Thr Val Lys Gly Lys Ala Leu Glu Val Ala
          -55 -50
                                               -45
Glu Tyr Leu Thr Pro Val Leu Lys Glu Ser Lys Phe Arg Glu Thr Gly
                           - 35
Val Ile Thr Pro Glu Glu Phe Val Ala Ala Gly Asp His Leu Val His
                       -20
His Cys Pro Thr Trp Gln Trp Ala Thr Gly Glu Glu Leu Lys Val Lys
                  - 5
Ala Tyr Leu Pro Thr Gly Lys Gln Phe Leu Val Thr Lys Asn Val Pro
Cys Tyr Lys Arg Cys Lys Gln Met Glu Tyr Ser Asp Glu Leu Glu Ala
  . 25
                         30
                                            35
Ile Ile Glu Glu Asp Asp Gly Asp Gly Gly Trp Val Asp Thr Tyr His
                      45
Asn Thr Gly Ile Thr Gly Ile Thr Glu Ala Val Lys Glu Ile Thr Leu
                  60
Glu Asn Lys Asp Asn Ile Arg Leu Gln Asp Cys Ser Ala Leu Cys Glu
                                 80
              75
Glu Glu Glu Asp Glu Asp Glu Gly Glu Ala Ala Asp Met Glu Glu Tyr
                              95
Glu Glu Ser Gly Leu Leu Glu Thr Asp Glu Ala Thr Leu Asp Thr Arg
                          110
                                             115
Lys Ile Val Glu Ala Cys Lys Ala Lys Thr Asp Ala Gly Gly Glu Asp
                       125
                                         130
Ala Ile Leu Gln Thr Arg Thr Tyr Asp Leu Tyr Ile Thr Tyr Asp Lys
                   140
                                      145
Tyr Tyr Gln Thr Pro Arg Leu Trp Leu Phe Gly Tyr Asp Glu Gln Arg
                                 160
              155
Gln Pro Leu Thr Val Glu His Met Tyr Glu Asp Ile Ser Gln Asp His
          170
                             175
Val Lys Lys Thr Val Thr Ile Glu Asn His Pro His Leu Pro Pro Pro
                                            195
       185
                          190
Pro Met Cys Ser Val His Pro Cys Arg His Ala Glu Val Met Lys Lys
                      205
                                          210
Ile Ile Glu Thr Val Ala Glu Gly Gly Glu Leu Gly Val His Met
                   220
                                      225
Tyr Leu Leu Ile Phe Leu Lys Phe Val Gln Ala Val Ile Pro Thr Ile
              235 240
Glu Tyr Asp Tyr Thr Arg His Phe Thr Met
           250
```

```
<210> 164
<211> 89
<212> PRT
<213> Homo sapiens
<220>
```

<221> SIGNAL <222> -80..-1

WO 99/31236 -125- PCT/IB98/02122

```
-25
       -30
Gln Leu Gly Arg Gly Leu Leu Ser Ala Cys Ala Pro Trp Gly Asp Gly
                   -10
Ser Thr Gln Pro Val Pro Leu Cys Ser
              5
<210> 165
<211> 98
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 165
Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu Ala Val Leu Ala Trp
                  -10
                                     - 5
Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg Met Lys Ser Arg Glu
                             10
Gln Gly Gly Arg Leu Gly Ala Glu Ser Arg Thr Leu Leu Val Ile Ala
                         25
    20
His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro Thr Val Leu Gly Leu
                     40
                                         45
Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys Phe Ser Ala Val Phe
                                     60
50 55
Arg Arg Glu Leu Ser Glu Tyr Thr Glu Gly Leu Thr Ser Glu Pro Leu
                                  75
Thr Ala
<210> 166
<211> 92
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -36..-1
<400> 166
Met Leu Val Thr Gln Gly Leu Val Tyr Gln Gly Tyr Leu Ala Ala Asn
   -35
                       -30
                                          -25
Ser Arg Phe Gly Ser Leu Pro Lys Val Ala Leu Ala Gly Leu Leu Gly
                                                       - 5
                  -15
                                     -10
-20
Phe Gly Leu Gly Lys Val Ser Tyr Ile Gly Val Cys Gln Ser Lys Phe
                                                 10
              1
His Phe Phe Glu Asp Gln Leu Arg Gly Ala Gly Phe Gly Pro Gln His
                          20
                                             25
Asn Arg His Cys Leu Leu Thr Cys Glu Glu Cys Lys Ile Lys His Gly
                      35
                                        40
Leu Ser Glu Lys Gly Asp Ser Gln Pro Ser Ala Ser
                   50
```

<210> 167 <211> 351

<212> PRT

PCT/IB98/02122

<213> Homo sapiens <220> <221> SIGNAL <222> -16..-1 <400> 167 Met Val Pro Phe Ile Tyr Leu Gln Ala His Phe Thr Leu Cys Ser Gly -15 -10 Trp Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr 10 Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile 25 Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr 4.0 4.5 Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu 55 Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Pro Glu Pro 75 70 Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser 90 85 Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu 100 105 110 Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu 120 125 Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr 135 Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met 150 155 Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr 170 165 Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser 190 185 180 Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu 200 205 Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile 220 215 Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser 230 235 Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp 245 250 Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser 265 260 Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val 275 280 285 Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys 295 300 His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Cys

```
<210> 168
<211> 138
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
```

<222> -47..-1

310

His Leu Gly His Gly Arg Leu Trp Leu Gln His Ser Thr Asp Arg

```
<400> 168
Met Glu Lys Phe Val Asp Pro Gly Asn His Asn Ser Gly Ile Asp Leu
             -40 -35
 - 4 5
Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu Leu Pro Phe Val Ser
                 -25
                           -20
Leu Gly Leu Met Cys Phe Gly Ala Leu Ile Gly Leu Cys Ala Cys Ile
-15 -10 -5
Cys Arg Ser Leu Tyr Pro Thr Ile Ala Thr Gly Ile Leu His Leu Leu
               10.
Ala Gly Leu Cys Thr Leu Gly Ser Val Ser Cys Tyr Val Ala Gly Ile
                     25 . 30
      20
Glu Leu Leu His Gln Lys Leu Glu Leu Pro Asp Asn Val Ser Gly Glu
               40 45
Phe Gly Trp Ser Phe Cys Leu Ala Cys Val Ser Ala Pro Leu Gln Phe
             55 60
Met Ala Ser Ala Leu Phe Ile Trp Ala Ala His Thr Asn Arg Arg Glu
                  75
            70
Tyr Thr Leu Met Lys Ala Tyr Arg Val Ala
       85 90
```

```
<210> 169
<211> 101
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -73..-1
<400> 169
Met Asn Leu Glu Arg Val Ser Asn Glu Glu Lys Leu Asn Leu Cys Arg
                               -60
    -70
                -65
Lys Tyr Tyr Leu Gly Gly Phe Ala Phe Leu Pro Phe Leu Trp Leu Val
                                       -45
                     -50
 -55
Asn Ile Phe Trp Phe Tyr Arg Glu Ala Phe Leu Val Pro Ala Tyr Thr
                                   -30
                 -35
Glu Gln Ser Gln Ile Lys Gly Tyr Val Trp Arg Ser Ala Val Gly Phe
                        -15
                -20
Leu Phe Trp Val Ile Val Leu Thr Ser Trp Ile Thr Ile Phe Gln Ile
            -5
                           1
Tyr Arg Pro Arg Trp Gly Ala Leu Gly Asp Tyr Leu Ser Phe Thr Ile
  10
Pro Leu Gly Thr Pro
  25
```

WO 99/31236 -128- PCT/IB98/02122

Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val -45 Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser -30 Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro -15 -10 Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His 20 Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu 35 Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys 50 Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe 70 65 Arg Glu Asn Val Leu Arg Asn Leu Ala Asp Lys Ala Phe Asp Arg Pro Ile Cys Glu Ala Leu Leu Asp Gln Arg Phe Phe Asn Gly Ile Gly Asn 100 105 Tyr Leu Arg Ala Glu Ile Leu Tyr Arg Leu Lys Ile Pro Pro Phe Glu 120 115 Lys Ala Arg Ser Val Leu Glu Ala Leu Gln Gln His Arg Pro Ser Pro 130 135 Glu Leu Thr Leu Ser Gln Lys Ile Arg Thr Lys Leu Gln Asn Ser Asp 150 145 Leu Leu Glu Leu Cys His Ser Val Pro Lys Glu Val Val Gln Leu Gly 165 160 Glu Ala Lys Asp Gly Ser Asn Leu Cys Phe Ser Lys

<210> 171 <211> 350 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -68..-1

<400> 171 Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu -60 - 65 Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser -30 -25 Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro -10 -15 Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His 20 Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu 35 Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys 5.5 50 Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Glr. Glu Tyr Gln Gln Phe Arg Leu Lys Ile Pro Pro Phe Glu Lys Ala Arg Ser Val Leu Glu Ala WO 99/31236 -129- PCT/IB98/02122

```
85 '
Leu Gln Gln His Arg Pro Ser Pro Glu Leu Thr Leu Ser Gln Lys Ile
                                         105
          100
Arg Thr Lys Leu Gln Asn Pro Asp Leu Leu Glu Leu Cys His Ser Val
                    115
                                     120
Pro Lys Glu Val Asp Gln Leu Gly Gly Arg Gly Tyr Gly Ser Glu Ser
                130
                                  135
Gly Glu Glu Asp Phe Ala Ala Phe Arg Ala Trp Leu Arg Cys Tyr Gly
                              150
             145
Met Pro Gly Met Ser Ser Leu Gln Asp Arg His Gly Arg Thr Ile Trp
                                            170
          160
                           165
Phe Gln Gly Asp Pro Gly Pro Leu Ala Pro Lys Gly Arg Lys Ser Arg
                                         185
                      180
      175
Lys Lys Lys Ser Lys Ala Thr Gln Leu Ser Pro Glu Asp Arg Val Glu
                               200
          195
  190
Asp Ala Leu Pro Pro Ser Lys Ala Pro Ser Lys Thr Arg Arg Ala Lys
                        215
               210
Arg Asp Leu Pro Lys Arg Thr Ala Thr Gln Arg Pro Glu Gly Th. Ser
                     230
          225
Leu Gln Gln Asp Pro Glu Ala Pro Thr Val Pro Lys Lys Gly Arg Arg
                                            250
                            245
         240
Lys Gly Arg Gln Ala Ala Ser Gly His Cys Arg Pro Arg Lys Val Lys
              260
Ala Asp Ile Pro Ser Leu Glu Pro Glu Gly Thr Ser Ala Ser
                     275
   270
```

<210> 172 <211> 390 <212> PRT

```
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -68..-1
<400> 172
Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu
          -65
                             -60
Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val
                       -45
    -50
Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser
                                         -25
                     - 30
Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro
                                  -10
                   -15
Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly
                     5
              1
Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His
                           20
       15
Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu
                                          40
                      35
Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys
                   50
                                     55
Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe
                                  70
Arg Glu Asn Val Leu Arg Asn Leu Ala Asp Lys Ala Phe Asp Arg Pro
                              85
Ile Cys Glu Ala Leu Leu Asp Gln Arg Phe Phe Asn Gly Ile Gly Asn
                                              105
                          100
Tyr Leu Arg Ala Glu Ile Leu Tyr Arg Leu Lys Ile Pro Pro Phe Glu
                                         120
    110
```

WO 99/31236 -130- PCT/IB98/02122

```
Lys Ala Arg Ser Val Leu Glu Ala Leu Gln Gln His Arg Pro Ser Pro
                  130
                                     135
Glu Leu Thr Leu Ser Gln Lys Ile Arg Thr Lys Leu Gln Asn Pro Asp
              145
                                  150
Leu Leu Glu Leu Cys His Ser Val Pro Lys Glu Val Val Gln Leu Gly
                              165
           160
Gly Arg Gly Tyr Gly Ser Glu Ser Gly Glu Glu Asp Phe Ala Ala Phe
                           180
                                             185
Arg Ala Trp Leu Arg Cys Tyr Gly Met Pro Gly Met Ser Ser Leu Gln
                       195
                                          200
Asp Arg His Gly Arg Thr Ile Trp Phe Gln Gly Asp Pro Gly Pro Leu
                  210
                                     215
Ala Pro Lys Gly Arg Lys Ser Arg Lys Lys Lys Ser Lys Ala Thr Gln
                                230
              225
Leu Ser Pro Glu Asp Arg Val Glu Asp Ala Leu Pro Pro Ser Lys Ala
                              245
          240
Pro Ser Arg Thr Arg Arg Ala Lys Arg Asp Leu Pro Lys Arg Thr Ala
                           260
                                    265
Thr Gln Arg Pro Glu Gly Thr Ser Leu Gln Gln Asp Pro Glu Ala Pro
                                        280
                       275
Thr Val Pro Lys Lys Gly Arg Arg Lys Gly Arg Gln Ala Ala Ser Gly
                                     295
                  290
His Cys Arg Pro Arg Lys Val Lys Ala Asp Ile Pro Ser Leu Glu Pro
                               310
              3 0 5
Glu Gly Thr Ser Ala Ser
           320
```

```
<210> 173
<211> 190
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -82..-1
```

<400> 173 Met Tyr Val Trp Pro Cys Ala Val Val Leu Ala Gln Tyr Leu Trp Phe -70 -75 -80 His Arg Arg Ser Leu Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala Gly -60 -65 Val Ser Leu Pro Gly Ile Leu Thr Ala Lys Cys Gly Ala Glu Val Ile -45 -40 Leu Ser Asp Ser Ser Glu Leu Pro His Cys Leu Glu Val Cys Arg Gln -30 -25 Ser Cys Gln Met Asn Asn Leu Pro His Leu Gln Val Val Gly Leu Thr -10 -15 Trp Gly His Ile Ser Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp Ile 10 Ile Leu Ala Ser Asp Val Phe Phe Glu Pro Glu Asp Phe Glu Asp Ile 20 25 Leu Ala Thr Ile Tyr Phe Leu Met His Lys Asn Pro Lys Val Gln Leu 40 Trp Ser Thr Tyr Gln Val Arg Ser Ala Asp Trp Ser Leu Glu Ala Leu 55 Leu Tyr Lys Trp Asp Met Lys Cys Val His Ile Pro Leu Glu Ser Phe 70 Asp Ala Asp Lys Glu Asp Ile Ala Glu Ser Thr Leu Pro Gly Arg His 85 Thr Val Glu Met Leu Val Ile Ser Phe Ala Lys Asp Ser Leu

105

95

· 1

100

<210> 174 <211> 285 <212> PRT <213> Homo sapiens

<220>

<221> SIGNAL <222> -232..-1

Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg
-200 -195 -190 -185
Val His Leu Met Gly Asp Asn Leu Cys Asn Asp Gly Ser Leu Leu

-180 -175 -170
Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg

-165 -160 -155
Leu Lys Gly Glu Ser Gln Val Phe Lys Lys Ala Val Val Leu His Val

-150 -145 -140 Leu Pro Glu Glu Pro Lys Glu Leu Met Val His Val Gly Gly Leu Ile

-135 -130 -125
Gln Met Gly Cys Val Phe Gln Ser Thr Glu Val Lys His Val Thr Lys
-120 -115 -110 -105

-120 -115 -110 -105
Val Glu Trp Ile Phe Ser Gly Arg Arg Ala Lys Glu Glu Ile Val Phe
-100 -95 -90

Arg Tyr Tyr His Lys Leu Arg Met Ser Ala Glu Tyr Ser Gln Ser Trp
-85 -80 -75

Gly His Phe Gln Asn Arg Val Asn Leu Val Gly Asp Ile Phe Arg Asn
-70 -65 -60

Asp Gly Ser Ile Met Leu Gln Gly Val Arg Glu Ser Asp Gly Gly Asn
-55 -50 -45

Val Leu His Val Ser Pro Glu Glu Pro Arg Thr Leu Val Thr Pro Ala
-20 -15 . -10

Ala Leu Arg Pro Leu Val Leu Gly Gly Asn Gln Leu Val Ile Val

Gly Ile Val Cys Ala Thr Ile Leu Leu Leu Pro Val Leu Ile Leu Ile
10 15 20 The Val Leu

Val Lys Lys Thr Cys Gly Asn Lys Ser Ser Val Asn Ser Thr Val Leu
25 30 40

Val Lys Asn Thr Lys Lys Thr Asn Pro Lys Lys Lys Lys 45 50

<210> 175 <211> 153 <212> PRT <213> Homo sapiens

```
2.0
                                2.5
Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg
                           40
Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu Leu
Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg
                                       75
                   70
Leu Lys Gly Glu Ser Gln Val Phe Lys Lys Ala Val Val Leu His Val
              85
                                  90
Leu Pro Glu Glu Pro Lys Glu Leu Met Val His Val Gly Gly Leu Ile
                               105
                                                  110
          100
Gln Met Gly Cys Val Phe Gln Ser Thr Glu Val Lys His Val Thr Lys
       115
                          120
                                               125
Val Glu Trp Ile Phe Ser Gly Arg Arg Ala Lys Val Thr Arg Arg Lys
                       135
His His Cys Val Arg Glu Gly Ser Gly
                   150
```

<210> 176 <211> 49 <212> PRT <213> Homo sapiens

Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu 10 Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val 25 30 Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro Ser Cys Pro Arg Phe Cys

<210> 177 <211> 99 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -24..-1

<400> 177 Met Lys Ser Ala Lys Leu Gly Phe Leu Leu Arg Phe Phe Ile Phe Cys -15 -20 Ser Leu Asn Thr Leu Leu Leu Gly Gly Val Asn Lys Ile Ala Glu Lys Ile Cys Gly Asp Leu Lys Asp Pro Cys Lys Leu Asp Met Asn Phe Gly 15 Ser Cys Tyr Glu Val His Phe Arg Tyr Phe Tyr Asn Arg Thr Ser Lys 35 30 Arg Cys Glu Thr Phe Val Phe Ser Gly Cys Asn Gly Asn Leu Asn Asn Phe Lys Leu Lys Ile Glu Arg Glu Val Ala Cys Val Ala Lys Tyr Lys Pro Pro Arg

<212> PRT

<213> Homo sapiens

```
<210> 178
<211> 95
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
<400> 178
Met Ala Ser Pro Ala Val Asn Arg Trp Lys Arg Pro Arg Leu Lys Pro
       -35
                          -30
                                           -25
Val Trp Pro Arg Arg Leu Glu Ser Trp Leu Leu Leu Asp Ala Leu Leu
                       -15
                                         -10
Arg Leu Gly Asp Thr Lys Lys Lys Arg Gln Pro Glu Ala Ala Thr Lys
- 5
                 1
                                  5
Ser Cys Val Arg Ser Ser Cys Gly Gly Pro Ser Gly Asp Gly Pro Pro
                           20
          15
Pro Cys Leu Gln Gln Pro Asp Pro Arg Ala Leu Ser Gln Ala Phe Ser
                          35
                                              40
Arg Ser Phe Pro Leu Phe Pro Ser Leu Ala Gly Lys Ser Met Ile
   45
                      50
<210> 179
<211> 121
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 179
Met Met Leu Pro Gln Trp Leu Leu Leu Phe Leu Leu Phe Phe Phe
                               -15
Leu Phe Leu Leu Thr Arg Gly Ser Leu Ser Pro Thr Lys Tyr Asn Leu
Leu Glu Leu Lys Glu Ser Cys Ile Arg Asn Gln Asp Cys Glu Thr Gly
                   15
                                      20
Cys Cys Gln Arg Ala Pro Asp Asn Cys Glu Ser His Cys Ala Glu Lys
              30
                                   35
Gly Ser Glu Gly Ser Leu Cys Gln Thr Gln Val Phe Phe Gly Gln Tyr
           45
                               50
Arg Ala Cys Pro Cys Leu Arg Asn Leu Thr Cys Ile Tyr Ser Lys Asn
                           65
                                               70
Glu Lys Trp Leu Ser Ile Ala Tyr Gly Arg Cys Gln Lys Ile Gly Arg
                       80
Gln Lys Leu Ala Lys Lys Met Phe Phe
<210> 180
<211> 59
```

<400> 180

Met Ile Leu Cys Phe Leu Leu Pro His His Arg Leu Gln Glu Ala Arg

<210> 181 <211> 86 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -14..-1 <400> 181 Met Val Ala Leu Asn Leu Ile Leu Val Pro Cys Cys Ala Ala Trp Cys -10 -5 Asp Pro Arg Arg Ile His Ser Gln Asp Asp Val Pro Arg Ser Ser Ala 10 15 Ala Asp Thr Gly Ser Ala Met Gln Arg Arg Glu Ala Trp Ala Gly Trp 20 25 30 Arg Arg Ser Gln Pro Phe Ser Val Gly Leu Pro Ser Ala Glu Arg Leu 45 35 40 Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg Ser Leu Val Gly Glu Gly 55 60 Tyr Arg Ile Cys Asp Leu

<210> 182 <211> 165 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -58..-1

<400> 182

70

Met Thr Arg Leu Cys Leu Pro Arg Pro Glu Ala Arg Glu Asp Pro Ile -55 -50 Pro Val Pro Pro Arg Gly Leu Gly Ala Gly Glu Gly Ser Gly Ser Pro -40 Val Arg Pro Pro Val Ser Thr Trp Gly Pro Ser Trp Ala Gln Leu Leu -15 -20 Asp Ser Val Leu Trp Leu Gly Ala Leu Gly Leu Thr Ile Gln Ala Val - 5 1 -10 Phe Ser Thr Thr Gly Pro Ala Leu Leu Leu Leu Val Ser Phe Leu 15 10 Thr Phe Asp Leu Leu His Arg Pro Ala Gly His Thr Leu Pro Gln Arg 25 30 Lys Leu Leu Thr Arg Gly Gln Ser Gln Gly Ala Gly Glu Gly Pro Gly 50 Gln Gln Glu Ala Leu Leu Gln Met Gly Thr Val Ser Gly Gln Leu 65 60 Ser Leu Gln Asp Ala Leu Leu Leu Leu Leu Met 3ly Leu Gly Pro Leu

```
80
Leu Arg Ala Cys Gly Met Pro Leu Thr Leu Leu Gly Leu Ala Phe Cys
     90
                      95
                                    100
Leu His Pro Trp Ala
     105
<210> 183
<211> 80
<212> PRT
<213 > Homo sapiens
<220>
<221> SIGNAL
<222> -35..-1
<400> 183
Met Pro Phe Gln Phe Gly Thr Gln Pro Arg Arg Phe Pro Val Glu Gly
-35 -30 -25 -20
Gly Asp Ser Ser Ile Glu Leu Glu Pro Gly Leu Ser Ser Ala Ala
            -15 -10 -5
Cys Asn Gly Lys Glu Met Ser Pro Thr Arg Gln Leu Arg Arg Cys Pro
         1 5 10
Gly Ser His Cys Leu Thr Ile Thr Asp Val Pro Val Thr Val Tyr Ala
                          25
15 20
Thr Thr Arg Lys Pro Pro Ala Gln Ser Ser Lys Glu Met His Pro Lys
                      40
            35
<210> 184
<211> 73
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 184
Met Ala Pro Gln Thr Leu Leu Pro Val Leu Val Leu Cys Val Leu Leu
-20 -15 -10
Leu Gln Ala Gln Gly Gly Tyr Arg Asp Lys Met Arg Met Gln Arg Ile
                         5
               1
-5
Lys Val Cys Glu Lys Arg Pro Ser Ile Asp Leu Cys Ile His His Cys
             20 25
        15
Ser Cys Phe Gln Lys Cys Glu Thr Asn Lys Ile Cys Cys Ser Ala Phe
                                     40
               35
Cys Gly Asn Ile Cys Met Ser Ile Leu
          50
  45
<210> 185
<211> 98
<212> PRT
<213> Homo sapiens
```

Met Leu Gly Ala Glu Thr Glu Glu Lys Leu Phe Asp Ala Pro Leu Ser

WO 99/31236 -136- PCT/IB98/02122 -

<210> 186 <211> 112 <212> PPT <213> Homo sapiens <220> <221> SIGNAL

<222> -21..-1

<400> 186 Met Glu Ser Arg Val Leu Leu Arg Thr Phe Cys Leu Ile Phe Gly Leu -15 Gly Ala Val Trp Gly Leu Gly Val Asp Pro Ser Leu Gln Ile Asp Val Leu Thr Glu Leu Glu Leu Gly Glu Ser Thr Thr Gly Val Arg Gln Val 20 Pro Gly Leu His Asn Gly Thr Lys Ala Phe Leu Phe Gln Asp Thr Pro 35 40 Arg Ser Ile Lys Ala Ser Thr Ala Thr Ala Glu Gln Phe Phe Gln Lys 55 50 Leu Arg Asn Lys His Glu Phe Thr Ile Leu Val Thr Leu Lys Gln Thr 65 His Leu Asn Ser Gly Val Ile Leu Ser Ile His His Leu Asp His Arg 80 . 85

<210> 187 <211> 70 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<222> -44..-1

```
<210> 188
<211> 92
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -13..-1
<400> 188
Met Leu Phe Ser Leu Ser Leu Leu Ser Asn Leu Asn Gln Ile Gly Ser
   -10 -5
Ser His Leu Asp Arg Pro His Ile Pro Gly Gln Ser Ala Gln Leu Phe
                 10
                                 15
Ile Tyr Gln Met Ser Ser Gln Gln Leu Gln Gln Gln Pro Ser Ala Asn
       25
                                30
20
Lys Lys Ala Gly Lys Ile His Asn Thr Pro Phe Ala Asn Gln Leu Asn
                     4.5
Pro Thr Gln His Leu Ala Lys Pro Phe Gln Gln Ile Leu Pro Gly Arg
              60
        55
Gln Ser Gly Ser Leu Thr Ser Pro Phe Leu Ala Cys
<210> 189
<211> 207
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -42..-1
<400> 189
Met His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala
   -40 -35 -30
Ile Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe
                     -20
Asp Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile
                         1 5
-10 -5
Leu Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser
                           15
          10
Ala Ile Tyr Ala Ser Gln Thr Glu Gln Glu Tyr Leu Lys Ile Glu Lys
    25 ' 30
Val Asp Leu Pro Leu Ile Asp Ser Leu Ile Arg Val Leu Gln Asn Met
  40 45
Glu Gln Cys Gln Lys Lys Pro Glu Asn Ser Ala Glu Ser Asn Thr Glu
                                 65
55 60
Glu Thr Lys Arg Thr Asp Leu Thr Gln Asp Asp Leu His Leu Lys Ile
                              80
Leu Lys Asp Ile Leu Cys Glu Phe Leu Ser Asn Ile Phe Gln Ala Leu
                     · 95
Thr Lys Glu Thr Val Ala Gln Gly Val Lys Glu Gly Gln Leu Ser Lys
                                         115
                       110
 Gln Lys Cys Ser Ser Ala Phe Gln Asn Leu Leu Pro Phe Tyr Ser Pro
                                      130
                    125
 Val Val Glu Asp Phe Ile Lys Ile Leu Arg Glu Val Asp Lys Ala Leu
                         145 150
 135 140
 Ala Asp Asp Leu Glu Lys Asn Phe Pro Ser Leu Lys Val Gln Thr
```

155 160 165

<210> 190 <211> 201 <212> PRT <213> Homo sapiens

<400> 190 Met Gln Val Ala Leu Lys Glu Asp Leu Asp Ala Leu Lys Glu Lys Phe 10 Arg Thr Met Glu Ser Asn Gln Lys Ser Ser Phe Gln Glu Ile Pro Lys 25 Leu Asn Glu Glu Leu Leu Ser Lys Gln Lys Gln Leu Glu Lys Ile Glu 40 Ser Gly Glu Met Gly Leu Asn Lys Val Trp Ile Asn Ile Thr Glu Met 55 Asn Lys Gln Ile Ser Leu Leu Thr Ser Ala Val Asn His Leu Lys Ala 75 Asn Val Lys Ser Ala Ala Asp Leu Ile Ser Leu Pro Thr Thr Val Glu 90 85 Gly Leu Gln Lys Ser Val Ala Ser Ile Gly Asn Thr Leu Asn Ser Val 105 100 His Leu Ala Val Glu Ala Leu Gln Lys Thr Val Asp Glu His Lys Lys 120 125 Thr Met Glu Leu Leu Gln Ser Asp Met Asn Gln His Phe Leu Lys Glu . 135 140 Thr Pro Gly Ser Asn Gln Ile Ile Pro Ser Pro Ser Ala Thr Ser Glu 150 155 Leu Asp Asn Lys Thr His Ser Glu Asn Leu Lys Gln Met Gly Asp Arg 175 165 170 Ser Ala Thr Leu Lys Arg Gln Ser Leu Asp Gln Val Thr Asn Arg Thr 185 180

<210> 191 <211> 379 <212> PRT <213> Homo sapiens

Asp Thr Val Lys Ile Gln Lys Lys

<220>
<221> SIGNAL
<222> -37..-1

<400> 191 Met Pro His Ser Ser Leu His Pro Ser Ile Pro Cys Pro Arg Gly His -30 -25 Gly Ala Gln Lys Ala Ala Leu Val Leu Leu Ser Ala Cys Leu Val Thr -15 -10 Leu Trp Gly Leu Gly Glu Pro Pro Glu His Thr Leu Arg Tyr Leu Val 1 5 Leu His Leu Ala Ser Leu Gln Leu Gly Leu Leu Leu Asn Gly Val Cys 20 15 Ser Leu Ala Glu Glu Leu Arg His Ile His Ser Arg Tyr Arg Gly Ser 35 40 Tyr Trp Arg Thr Val Arg Ala Cys Leu Gly Cys Pro Leu Arg Arg Gly 50

Ala Leu Leu Leu Ser Ile Tyr Phe Tyr Tyr Ser Leu Pro Asn Ala

60 65 70 75
Val Gly Pro Pro Phe Thr Trp Met Leu Ala Leu Leu Gly Leu Ser Gln

80 85 90 Ala Leu Asn Ile Leu Leu Gly Leu Lys Gly Leu Ala Pro Ala Glu Ile
95 100 105

Ser Ala Val Cys Glu Lys Gly Asn Phe Asn Val Ala His Gly Leu Ala 110 115 120

Trp Ser Tyr Tyr Ile Gly Tyr Leu Arg Leu Ile Leu Pro Glu Leu Gln
125 130 135

Ala Arg Ile Arg Thr Tyr Asn Gln His Tyr Asn Asn Leu Leu Arg Gly 140 145 150 150

Ala Val Ser Gln Arg Leu Tyr Ile Leu Leu Pro Leu Asp Cys Gly Val 160 165 170

Pro Asp Asn Leu Ser Met Ala Asp Pro Asn Ile Arg Phe Leu Asp Lys 175 180 185

Leu Pro Gln Gln Thr Gly Asp Arg Ala Gly Ile Lys Asp Arg Val Tyr 190 195 200

Ser Asn Ser Ile Tyr Glu Leu Leu Glu Asn Gly Gln Arg Ala Gly Thr 205 210 215

Cys Val Leu Glu Tyr Ala Thr Pro Leu Gln Thr Leu Phe Ala Met Ser
220 235 230 235

Gln Tyr Ser Gln Ala Gly Phe Ser Arg Glu Asp Arg Leu Glu Gln Ala 240 245 250

Lys Leu Phe Cys Arg Thr Leu Glu Asp Ile Leu Ala Asp Ala Pro Glu 255 260 265

Ser Gln Asn Asn Cys Arg Leu Ile Ala Tyr Gln Glu Pro Ala Asp Asp 270 275 280

Ser Ser Phe Ser Leu Ser Gln Glu Val Leu Arg His Leu Arg Gln Glu 285 290 295

Glu Lys Glu Glu Val Thr Val Gly Ser Leu Lys Thr Ser Ala Val Pro 300 305 310 315

Ser Thr Ser Thr Met Ser Gln Glu Pro Glu Leu Leu Leu Ser Gly Met
320 325 330

Gly Lys Pro Leu Pro Leu Arg Thr Asp Phe Ser 335 340

<210> 192

<211> 112

<212> PRT

<213> Homo sapiens

<400> 192

Met Pro Ser Glu Gly Arg Cys Trp Glu Thr Leu Lys Ala Leu Arg Ser

1 5 10 15

Ser Asp Lys Gly Arg Leu Cys Tyr Tyr Arg Asp Trp Leu Leu Arg Arg

Glu Asp Val Leu Glu Glu Cys Met Ser Leu Pro Lys Leu Ser Ser Tyr 35 40 45

Ser Gly Trp Val Val Glu His Val Leu Pro His Met Gln Glu Asn Gln
50 55 60

Pro Leu Ser Glu Thr Ser Pro Ser Ser Thr Ser Ala Ser Ala Leu Asp
65 70 75 80

Gln Pro Ser Phe Val Pro Lys Ser Pro Asp Ala Ser Ser Ala Phe Ser 85 90 95

Pro Ala Ser Pro Ala Thr Pro Asn Gly Thr Lys Gly Lys Lys Lys Lys Lys 100 105 110

```
WO 99/31236
                                      -140-
<211> 43
<212> PRT
<213> Homo sapiens
<400> 193
Ser Leu Pro Gln Ala Leu Trp Phe Gln Phe Phe Tyr His Ser Gly Ser
                                    10
Ser Leu Glu Ser Pro Gly Met Leu Asn Gly Pro Phe Gln His Arg Asn
           20
                                25
Ser Arg Ile Met Thr His Arg Ser Ala Glu Lys
        35
                            40
<210> 194
<211> 51
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 194
Met Leu Arg Ile Ala Leu Thr Leu Ile Pro Ser Met Leu Ser Arg Ala
                        -10
    -15
Ala Gly Trp Cys Trp Tyr Lys Glu Pro Thr Gln Gln Phe Ser Tyr Leu
                                    10
Cys Leu Pro Cys Leu Ser Trp Asn Lys Lys Gly Asn Val Leu Gln Leu
Pro Asn Phe
       35
<210> 195
<211> 244
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
Met Ala Asn Pro Lys Leu Leu Gly Leu Glu Leu Ser Glu Ala Glu Ala
                                -10
            -15
Ile Gly Ala Asp Ser Ala Arg Phe Glu Glu Leu Leu Gln Ala Ser
```

 Met
 Ala
 Asn
 Pro
 Lys
 Leu
 Leu
 Gly
 Leu
 Glu
 Leu
 Glu
 Leu
 Ser
 Glu
 Ala
 Asp
 Ser
 Ala
 Arg
 Phe
 Glu
 Glu
 Leu
 Leu
 Leu
 Gln
 Ala
 Ser

 Lys
 Glu
 Leu
 Glu
 Asn
 Ser
 Ala
 Arg
 Phe
 Glu
 Leu
 Leu
 Leu
 Glu
 Asn
 Ile
 Arg
 Pro
 Glu
 Ser
 Thr
 Glu
 Ser
 Thr
 Glu
 Glu
 Glu
 Glu
 Glu
 Glu
 Leu
 Asn
 Ile
 Asn
 Ile
 Lys
 Thr
 Asn
 Ser
 Ser
 Ile
 I

120 115 Ile Ala Arg Glu Gly Leu Glu Asp Ile Tyr Asn Leu Gln Leu Asn Pro 135 140 Glu Trp Arg Met Met Lys Asn Arg Pro Phe Met Gly Ser Ile Ser Gln 150 155 Gln Asn Ile Arg Ser Glu Gln Arg Pro Arg Ile Gln Glu Leu Gly Asp 170 165 Leu Tyr Thr Pro Ala Pro Gly Arg Ala Glu Ser Gly Pro Glu Lys Pro 180 185 His Leu Asn Leu Trp Leu Glu Ala Pro Asp Leu Leu Leu Ala Glu Val 200 195 Asp Leu Pro Lys Leu Asp Gly Ala Leu Gly Leu Ser Leu Glu Ile Gly 210 215 Arg Thr Ala Trp 225

<210> 196 <211> 353 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -34..-1

<400> 196 Met Glu Arg Gly Leu Lys Ser Ala Asp Pro Arg Asp Gly Thr Gly Tyr -25 -30 Thr Gly Trp Ala Gly Ile Ala Val Leu Tyr Leu His Leu Tyr Asp Val -10 -15 Phe Gly Asp Pro Ala Tyr Leu Gln Leu Ala His Gly Tyr Val Lys Gln 10 Ser Leu Asn Cys Leu Thr Lys Arg Ser Ile Thr Phe Leu Cys Gly Asp 20 25 Ala Gly Pro Leu Ala Val Ala Ala Val Leu Tyr His Lys Met Asn Asn 40 35 Glu Lys Gln Ala Glu Asp Cys Ile Thr Arg Leu Ile His Leu Asn Lys 55 Ile Asp Pro His Ala Pro Asn Glu Met Leu Tyr Gly Arg Ile Gly Tyr 70 Ile Tyr Ala Leu Leu Phe Val Asn Lys Asn Phe Gly Val Glu Lys Thr 90 85 Pro Gln Ser His Ile Gln Gln Ile Cys Glu Thr Ile Leu Thr Ser Gly 105 100 Glu Asn Leu Ala Arg Lys Arg Asn Phe Thr Ala Lys Ser Pro Leu Met 120 Tyr Glu Trp Tyr Gln Glu Tyr Tyr Val Gly Ala Ala His Gly Leu Ala 135 130 Gly Ile Tyr Tyr Tyr Leu Met Gln Pro Ser Leu Gln Val Ser Gln Gly 155 150 145 Lys Leu His Ser Leu Val Lys Pro Ser Val Asp Tyr Val Cys Gln Leu 165 170 Lys Phe Pro Ser Gly Asn Tyr Pro Pro Cys Ile Gly Asp Asn Arg Asp 185 180 Leu Leu Val His Trp Cys His Gly Ala Pro Gly Val Ile Tyr Met Leu 200 195 Ile Gln Ala Tyr Lys Val Phe Arg Glu Glu Lys Tyr Leu Cys Asp Ala 215 210 Tyr Gln Cys Ala Asp Val Ile Trp Gln Tyr Gly Leu Leu Lys Lys Gly 230

```
Tyr Gly Leu Cys His Gly Ser Ala Gly Asn Ala Tyr Ala Phe Leu Thr
240

Leu Tyr Asn Leu Thr Gln Asp Met Lys Tyr Leu Tyr Arg Ala Cys Lys
255

Phe Ala Glu Trp Cys Leu Glu Tyr Gly Glu His Gly Cys Arg Thr
275

Asp Thr Pro Phe Ser Leu Phe Glu Gly Met Ala Gly Thr Ile Tyr Phe
290

Leu Ala Asp Leu Leu Val Pro Thr Lys Ala Arg Phe Pro Ala Phe Glu
305

Leu Cu Sin Find Cys His Gly Ser Leu Change Sin Find Cys Cys Arg Thr
310

The Ala Asp Leu Leu Val Pro Thr Lys Ala Arg Phe Pro Ala Phe Glu
310

Leu Cu Sin Find Cys Leu Change Sin Find Cys Arg Thr
315

Leu Cu Sin Find Cys Leu Change Sin Find Cys Arg Cys Arg Thr
316

The Ala Asp Leu Leu Val Pro Thr Lys Ala Arg Phe Pro Ala Phe Glu
315

Leu Cu Sin Find Cys Cys Cys Arg Thr
316

The Ala Asp Leu Leu Val Pro Thr Lys Ala Arg Phe Pro Ala Phe Glu
316
```

<210> 197 <211> 30 <212> PRT <213> Homo sapiens

<210> 198 <211> 112 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -48..-1

<400> 198 Met Gln Asp Thr Gly Ser Val Val Pro Leu His Trp Phe Gly Phe Gly -40 -45 Tyr Ala Ala Leu Val Ala Ser Gly Gly Ile Ile Gly Tyr Val Lys Ala -20 -25 -30 Gly Ser Val Pro Ser Leu Ala Ala Gly Leu Leu Phe Gly Ser Leu Ala -10 -15 Gly Leu Gly Ala Tyr Gln Leu Ser Gln Asp Pro Arg Asn Val Trp Val 10 Phe Leu Ala Thr Ser Gly Thr Leu Ala Gly Ile Met Gly Met Arg Phe 25 20 Tyr His Ser Gly Lys Phe Met Pro Ala Gly Leu Ile Ala Gly Ala Ser 45 40 Leu Leu Met Val Ala Lys Val Gly Val Ser Met Phe Asn Arg Pro His 55

<210> 199 <211> 54 <212> PRT <213> Homo sapiens

WO 99/31236 -143 - PCT/IB98/02122

```
      Pro
      Arg
      Trp
      His
      Arg
      Leu
      Pro
      Pro
      Gln
      Ser
      Leu
      Gln
      His
      His
      Gln
      Tyr

      Cys
      Gln
      Arg
      Arg
      Trp
      Pro
      Asp
      Arg
      Arg
      Cys
      Leu
      Gln
      Ser
      His
      Thr
      Gln

      Ser
      Ser
      Gly
      His
      Leu
      Pro
      From the proper of the
```

```
<210> 200
<211> 151
<212> PRT
<213> Homo sapiens
                              ، نے زہ ،
<220>
<221> SIGNAL
<222> -21..-1
<400> 200
Met Ala Ala Ser Thr Ser Met Xaa Pro Val Ala Val Thr Ala Ala Val
 -20 -15
                                        -10
Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu Arg Glu Ile
                                5
                 1
Lys Lys Gln Leu Leu Ile Ala Gly Leu Thr Arg Glu Arg Gly Leu
                             20
Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser Leu Pro Ala
                          35
Leu Pro Xaa Gly Gln Leu Gln Pro Pro Pro Pro Ile Thr Glu Glu Asp
                       50
Ala Gln Asp Met Asp Ala Tyr Thr Leu Ala Lys Ala Tyr Phe Asp Val
                                   . 70
                   65
Lys Glu Tyr Asp Arg Ala Ala His Phe Leu His Gly Cys Asn Ser Lys
                                 85
Lys Ala Tyr Phe Leu Tyr Met Tyr Ser Arg Tyr Leu Val Arg Ala Ile
                           100
Leu Lys Cys His Ser Ala Phe Ser Glu Thr Ser Ile Phe Arg Thr Asn
               115
     110
Gly Lys Val Lys Ser Phe Lys
   125
```

<210> 201 <211> 228 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -25..-1 Met Ser Met Ala Val Glu Thr Phe Gly Phe Phe Met Ala Thr Val Gly -15 -20 Leu Leu Met Leu Gly Val Thr Leu Pro Asn Ser Tyr Trp Arg Val Ser - 5 Thr Val His Gly Asn Val Ile Thr Thr Asn Thr Ile Phe Glu Asn Leu 15 Trp Phe Ser Cys Ala Thr Asp Ser Leu Gly Val Tyr Asn Cys Trp Glu 30 35 Phe Pro Ser Met Leu Ala Leu Ser Gly Tyr Ile Gln Ala Cys Arg Ala

```
Leu Met Ile Thr Ala Ile Leu Leu Gly Phe Leu Gly Leu Leu Leu Gly
Ile Ala Gly Leu Arg Cys Thr Asn Ile Gly Gly Leu Glu Leu Ser Arg
                          80
Lys Ala Lys Leu Ala Ala Thr Ala Gly Ala Pro His Ile Leu Ala Gly
   90
                       95
                                       100
Ile Cys Gly Met Val Ala Ile Ser Trp Tyr Ala Phe Asn Ile Thr Arg
                   110
                             115
Asp Phe Phe Asp Pro Leu Tyr Pro Gly Thr Lys Tyr Glu Leu Gly Pro
                               130
120
       125
Ala Leu Tyr Leu Gly Trp Ser Ala Ser Leu Ile Ser Ile Leu Gly Gly
                    145 150
            140
Leu Cys Leu Cys Ser Ala Cys Cys Cys Gly Ser Asp Glu Asp Pro Ala
       155 160
Ala Ser Ala Arg Arg Pro Tyr Gln Ala Pro Val Ser Val Met Pro Val
                      175
                                 180
     170
Ala Thr Ser Asp Gln Glu Gly Asp Ser Ser Phe Gly Lys Tyr Gly Arg
                           195
                   190
Asn Ala Tyr Val
200
```

<210> 202 <211> 64 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -47..-1

<210> 203
<211> 146
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -31..-1

<210> 204 <211> 87 <212> PRT <213> Homo sapiens

<210> 205
<211> 40
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1
<400> 205

85

Met Arg Thr Leu Phe Gly Ala Val Arg Ala Pro Phe Ser Ser Leu Thr
-25
-20
-15

Leu Leu Leu Ile Thr Pro Ser Pro Ser Pro Leu Leu Phe Asp Arg Gly
-10
-5

Leu Ser Leu Arg Ser Ala Met Ser

<210> 206 <211> 154 <212> PRT <213> Homo sapiens

<400> 206 Met Gly Ser Leu Ser Gly Leu Arg Leu Ala Ala Gly Ser Cys Phe Arg

```
Leu Cys Glu Arg Asp Val Ser Ser Ser Leu Arg Leu Thr Arg Ser Ser
Asp Leu Lys Arg Ile Asn Gly Phe Cys Thr Lys Pro Gln Glu Ser Pro
                           40
Gly Ala Pro Ser Arg Thr Tyr Asn Arg Val Pro Leu His Lys Pro Thr
                      55
Asp Trp Gln Lys Lys Ile Leu Ile Trp Ser Gly Arg Phe Lys Lys Glu
                                     75
                  70
Asp Glu Ile Pro Glu Thr Val Ser Leu Glu Met Leu Asp Ala Ala Lys
                                  90
            85
Asn Lys Met Arg Val Lys Ser Ser Tyr Leu Met Ile Ala Leu Thr Val
                              105
           100
Val Gly Cys Ile Phe Met Val Ile Glu Gly Lys Lys Ala Ala Gln Arg
                                             125
       115
                        120
His Glu Thr Leu Thr Ser Leu Asn Leu Glu Lys Lys Ala Arg Leu Lys
                      135
Glu Glu Ala Ala Met Lys Ala Lys Thr Glu
                   150
```

<210> 207 <211> 101 <212> PRT <213> Homo sapiens

<400> 207 Met Val Cys Glu Lys Cys Glu Lys Lys Leu Gly Thr Val Ile Thr Pro 10 Asp Thr Trp Lys Asp Gly Ala Arg Asn Thr Thr Glu Ser Gly Gly Arg 20 Lys Leu Asn Lys Asn Lys Ala Leu Thr Ser Lys Lys Ala Arg Phe Asp 40 35 Pro Tyr Gly Lys Asn Lys Phe Ser Thr Cys Arg Ile Cys Lys Ser Ser 55 Val His Gln Pro Gly Ser His Tyr Cys Gln Gly Cys Ala Tyr Lys Lys 75 70 Gly Ile Cys Ala Met Cys Gly Lys Lys Val Leu Asp Thr Lys Asn Tyr 90 Lys Gln Thr Ser Val

<210> 208 <211> 456 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -22..-1

100

```
35
Glu Glu Glu Glu Glu Arg Lys Lys Cys Pro Lys Lys Ala Ser
45 50 55
                      50
Phe Ala Ser Ala Ser Ala Glu Val Gly Lys Lys Gly Lys Lys Cys
                   65
Gln Lys Gln Gly Pro Pro Cys Ser Asp Ser Glu Glu Glu Val Glu Arg
                              85
Lys Lys Lys Cys His Lys Gln Ala Leu Val Gly Ser Asp Ser Ala Glu
                             100
             95
Asp Glu Lys Arg Lys Arg Lys Cys Gln Lys His Ala Pro Ile Asn Ser
                                           120
                         115
          110
Ala Gln His Leu Asp Asn Val Asp Gln Thr Gly Pro Lys Ala Trp Lys
                      130
                            135
Gly Ser Thr Thr Asn Asp Pro Pro Lys Gln Ser Pro Gly Ser Thr Ser
                                    150
           . 145
Pro Lys Pro Pro His Thr Leu Ser Arg Lys Gln Trp Arg Asn Arg Gln
      160
                                 165
Lys Asn Lys Arg Arg Cys Lys Asn Lys Phe Gln Pro Pro Gln Val Pro
                              180
             175
Asp Gln Ala Pro Ala Glu Ala Pro Thr Glu Lys Thr Glu Val Ser Pro
          190
                         195
Val Pro Arg Thr Asp Ser His Gly Ala Arg Ala Gly Ala Leu Arg Ala
           210
                                215
    205
Arg Met Ala Gln Arg Leu Asp Gly Ala Arg Phe Arg Tyr Leu Asn Glu
            225 230
Gln Leu Tyr Ser Gly Pro Ser Ser Ala Ala Gln Arg Leu Phe Gln Glu
                                  245
         240
Asp Pro Glu Ala Phe Leu Leu Tyr His Arg Gly Phe Gln Ser Gln Val
             255 · 260
Lys Lys Trp Pro Leu Gln Pro Val Asp Arg Ile Ala Arg Asp Leu Arg
          270 275
Gln Arg Pro Ala Ser Leu Val Val Ala Asp Phe Gly Cys Gly Asp Cys
       285 290
                                        295
Arg Leu Ala Ser Ser Ile Arg Asn Pro Val His Cys Phe Asp Leu Ala
                             310
                    305
Ser Leu Asp Pro Arg Val Thr Val Cys Asp Met Ala Gln Val Pro Leu
                                  325
                320
Glu Asp Glu Ser Val Asp Val Ala Val Phe Cys Leu Ser Leu Met Gly
                               340
             335
Thr Asn Ile Arg Asp Phe Leu Glu Glu Ala Asn Arg Val Leu Lys Pro
                           355
          350
Gly Gly Leu Leu Lys Val Ala Glu Val Ser Ser Arg Phe Glu Asp Val
                        370
Arg Thr Phe Leu Arg Ala Val Thr Lys Leu Gly Phe Lys Ile Val Ser
                                     390
                    385
Lys Asp Leu Thr Asn Ser His Phe Phe Leu Phe Asp Phe Gln Lys Thr
                          405
        400
Gly Pro Pro Leu Val Gly Pro Lys Ala Gln Leu Ser Gly Leu Gln Leu
                        420
             415
Gln Pro Cys Leu Tyr Lys Arg Arg
```

```
<210> 209
<211> 98
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
```

<222> -17..-1

```
<400> 209
Met Pro Ser Ser Phe Phe Leu Leu Leu Gln Phe Phe Leu Arg Ile Asp
                              - 5
              -10
    -15
Gly Val Leu Ile Arg Met Asn Asp Thr Arg Leu Tyr His Glu Ala Asp
             5
                                  10
Lys Thr Tyr Met Leu Arg Glu Tyr Thr Ser Arg Glu Ser Lys Ile Ser
          20
                              25
Ser Leu Met His Val Pro Pro Ser Leu Phe Thr Glu Pro Asn Glu Ile
                         40
Ser Gln Tyr Leu Pro Ile Lys Glu Ala Val Cys Glu Lys Leu Ile Phe
                      55
     50
Pro Glu Arg Ile Asp Pro Asn Pro Ala Asp Ser Gln Lys Ser Thr Gln
                    70
Val Glu
80
```

<210> 210 <211> 83 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -29..-1

<210> 211 <211> 229 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -23..-1

50 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr 65 Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe 80 Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn 100 95 Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr 115 110 Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile 130 135 125 Ser Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu 150 145 Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe 165 155 160 Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val 175 180 170 Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys 195 190 Arg Lys Ser Arg Thr 205

<210> 212 <211> 152 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

<400> 212 Met Ala Gln Leu Gly Ala Val Val Ala Val Ala Ser Ser Phe Phe Cys -10 -15 Ala Ser Leu Phe Ser Ala Val His Lys Ile Glu Glu Gly His Ile Gly 1 Val Tyr Tyr Arg Gly Gly Ala Leu Leu Thr Ser Thr Ser Gly Pro Gly 20 15 Phe His Leu Met Leu Pro Phe Ile Thr Ser Tyr Lys Ser Val Gln Thr 40 35 Thr Leu Gln Thr Asp Glu Val Lys Asn Val Pro Cys Gly Thr Ser Gly 55 50 Gly Val Met Ile Tyr Phe Asp Arg Ile Glu Val Val Asn Phe Leu Val 70 65 Pro Asn Ala Val His Asp Ile Val Lys Asn Tyr Thr Ala Asp Tyr Asp 85 Lys Ala Leu Ile Phe Asn Lys Ile His His Glu Leu Asn Gln Phe Cys 100 Ser Val His Thr Leu Gln Glu Val Tyr Ile Glu Leu Phe Gly Leu Glu 110 115 Asn Asp Phe Ser Gln Glu Ser Ser 125

<210> 213 <211> 179 <212> PRT <213> Homma sapiens

```
<221> SIGNAL
<222> -54..-1
<400> 213
Met Ala Ala Ser Glu Ala Ala Val Val Ser Ser Pro Ser Leu Lys Thr
            -50
                               - 45
Asp Thr Ser Pro Val Leu Glu Thr Ala Gly Thr Val Ala Ala Met Ala
                              -30
          - 35
                                                -25
Ala Thr Pro Ser Ala Arg Ala Ala Ala Ala Val Val Ala Ala Ala Ala
                          -15
Arg Thr Gly Ser Glu Ala Arg Val Ser Lys Ala Ala Leu Ala Thr Lys
 -5 . 1
                                   5
                                              10
Leu Leu Ser Leu Ser Gly Val Phe Ala Val His Lys Pro Lys Gly Pro
                                 20
            15
Thr Ser Ala Glu Leu Leu Asn Arg Leu Lys Glu Lys Leu Leu Ala Glu
                              35
Ala Gly Met Pro Ser Pro Glu Trp Thr Lys Arg Lys Lys Gln Thr Leu
                          50
Lys Ile Gly His Gly Gly Thr Leu Asp Ser Ala Ala Arg Gly Val Leu
Val Val Gly Ile Gly Ser Gly Thr Lys Met Leu Thr Ser Met Leu Ser
                  80
                                     85
Gly Ser Lys Arg Tyr Thr Ala Ile Gly Glu Leu Gly Lys Ala Thr Asp
                                100
             95
Thr Leu Asp Ser Thr Gly Lys Val Thr Glu Glu Lys Pro Tyr Gly Met
                            115
Asn Leu Ile
      125
```

<210> 214 <211> 269 <212> PRT <213> Homo sapiens <220: <221> SIGNAL <222> -92..-1 <400> 214

<220>

Met Ile Thr His Val Thr Leu Glu Asp Ala Leu Ser Asn Val Asp Leu -85 -90 Leu Glu Glu Leu Pro Leu Pro Asp Gln Gln Pro Cys Ile Glu Pro Pro -70 -65 Pro Ser Ser Ile Met Tyr Gln Ala Asn Phe Asp Thr Asn Phe Glu Asp -55 -50 Arg Asn Ala Phe Val Thr Gly Ile Ala Arg Tyr Ile Glu Gln Ala Thr -40 -35 Val His Ser Ser Met Asn Glu Met Leu Glu Glu Gly His Glu Tyr Ala -20 -25 Val Met Leu Tyr Thr Trp Arg Ser Cys Ser Arg Ala Ile Pro Gln Val - 5 Lys Cys Asn Glu Gln Pro Asn Arg Val Glu Ile Tyr Glu Lys Thr Val 10 15 Glu Val Leu Glu Pro Glu Val Thr Lys Leu Met Lys Phe Met Tyr Phe 25 30 Gln Arg Lys Ala Ile Glu Arg Phe Cys Ser Glu Val Lys Arg Leu Cys 45 His Ala Glu Arg Arg Lys Asp Phe Val Ser Glu Ala Tyr Leu Leu Thr 60

<210> 215 <211> 135 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -22..-1

<400> 215

Met Gln Thr Val Tyr Tyr Gly Ser Leu Gly Leu Trp Leu Ala Leu Val -20 -15 -- -10. Asp Gly Leu Val Arg Ser Ser Pro Ser Leu Asp Gln Met Phe Asp Ala -5 1 Glu Ile Leu Gly Phe Ser Thr Pro Pro Gly Arg Leu Ser Met Met Ser 20 15 Phe Ile Phe Asn Ala Leu Thr Cys Ala Leu Gly Leu Leu Tyr Phe Ile . 30 35 40 Arg Arg Gly Lys Gln Cys Leu Asp Phe Thr Val Thr Val His Phe Phe 50 45 His Leu Leu Gly Cys Trp Phe Tyr Ser Ser Arg Phe Pro Ser Ala Leu 65 70 Thr Trp Trp Leu Val Gln Ala Val Cys Ile Ala Leu Met Ala Val Ile 85 90 80 Gly Glu Tyr Leu Cys Met Arg Thr Glu Leu Lys Glu Ile Pro Leu Asn 100 95 Ser Ala Pro Lys Ser Asn Val

<210> 216 <211> 67 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -38..-1

110

<210> 217 <211> 125 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -54..-1

<400> 217

Met Ala Asp Glu Glu Leu Glu Ala Leu Arg Arg Gln Arg Leu Ala Glu -50 -45 Leu Gln Ala Lys His Gly Asp Pro Gly Asp Ala Ala Gln Gln Glu Ala - 35 -30 Lys His Arg Glu Ala Glu Met Arg Asn Ser Ile Leu Ala Gln Val Leu -20 -15 -10 Asp Gln Ser Ala Arg Ala Arg Leu Ser Asn Leu Ala Leu Val Lys Pro Glu Lys Thr Lys Ala Val Glu Asn Tyr Leu Ile Gln Met Ala Arg Tyr Gly Gln Leu Ser Glu Lys Val Ser Glu Gln Gly Leu Ile Glu Ile Leu 35 Lys Lys Val Ser Gln Gln Thr Glu Lys Thr Thr Thr Val Lys Phe Asn 50 Arg Arg Lys Val Met Asp Ser Asp Glu Asp Asp Asp Tyr

<210> 218 <211> 376 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

Thr Glu Thr Met Ser Ser Leu Ser Pro Gly Arg Pro Trp Gln Thr Lys

```
100
Leu Ser Ser Ala Gly Leu Ile Tyr Leu His Phe Gly His Lys Leu Leu
                          115
                                             120
Ala Gln Leu Leu Gly Thr Ser Glu Glu Asp Ser Met Val Gly Thr Leu
                     130
                                         135
Tyr Asp Lys Met Tyr Glu Asn Phe Val Glu Glu Val Asp Ala Val Asp
                                      150
                  145
Asn Gly Ile Ser Gln Trp Ala Glu Gly Glu Pro Arg Tyr Ala Leu Thr
              160
                                 165
Thr Thr Leu Ser Ala Arg Val Ala Arg Leu Asn Pro Thr Trp Asn His
                             180
          175
Pro Asp Gln Asp Thr Glu Ala Gly Phe Lys Arg Ala Met Asp Leu Val
                         195
                                            200
Gln Glu Glu Phe Leu Gln Arg Leu Asp Phe Tyr Gln His Ser Trp Leu
                  210
                                        215
Pro Ala Arg Ala Leu Val Glu Glu Ala Leu Ala Gln Arg Phe Gln Val
                  225
                                      230
Asp Pro Ser Gly Glu Ile Val Glu Leu Ala Lys Gly Ala Cys Fro Trp
                                  245
Lys Glu His Leu Tyr His Leu Glu Ser Gly Leu Ser Pro Pro Val Ala
           255
                             260
Ile Phe Phe Val Ile Tyr Thr Asp Gln Ala Gly Gln Trp Arg Ile Gln
                          275
Cys Val Pro Lys Glu Pro His Ser Phe Gln Ser Arg Leu Pro Leu Pro
                     290
                                        295
Glu Pro Trp Arg Gly Leu Arg Asp Glu Ala Leu Asp Gln Val Ser Gly
                 305
                                     310
Ile Pro Gly Cys Ile Phe Val His Ala Ser Gly Phe Ile Gly Gly His
                                 325
              320
Arg Thr Arg Glu Gly Ala Leu Ser Met Ala Arg Ala Thr Leu Ala Gln
           335
                    340
Arg Ser Tyr Leu Pro Gln Ile Ser
      350
```

```
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -30..-1
<400> 219
Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His Leu Leu Val
                 -25
                                       -20
Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala Ala Ala Pro
                                   - 5
               -10
Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu Thr Gly Leu
                           10
Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys Gly Asn Leu
                       25
                                          30
Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp Phe Arg Gly
                                       45
                   40
Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His Gln Leu Gly
               55
Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val Pro Arg Met
```

Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr Asp Ser Phe

<210> 219 <211> 211

```
His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile Lys Leu Pro
                      105
Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His Trp Leu Ser
                 120
                                    125
115
Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu Arg Lys Gly
             135
                                140
Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser Ser His Ser
                                             160
         150
                            155
Arg Leu Ser Pro Arg Lys Thr His Leu Leu Tyr Ile Leu Arg Pro Ser
                170
                                            175
     165
Arg Gln Leu
  180
```

<210> 220 <211> 154 <212> PRT <213> Homo sapiens <221> SIGNAL <222> -60..-1 <400> 220 Met Gly Ser Lys Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu -55 -50 Arg Gln Arg Arg Gln Lys Leu Leu Leu Ala Gln Leu His His Arg Lys -35 -40 Arg Val Lys Ala Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu -20 -15 -25 Val Arg Arg Thr Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln - 5 -10 Cys Trp Trp Arg Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln 15 10 Ala Leu Leu Arg Val Tyr Val Ile Gln Glu Gln Ala Thr Val Lys Leu 25 30 Gln Ser Cys Ile Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met 45 Cys Asn Ala Leu Cys Leu Phe Gln Val Pro Glu Ser Ser Leu Ala Phe 60 Gln Thr Asp Gly Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln Pro Glu Phe His Ile Glu Ile Leu Ser Ile

<210> 222 <211> 346 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1

<400> 222 Met Ala Met Ala Gln Lys Leu Ser His Leu Leu Pro Ser Leu Arg Gln -10 -15 Val Ile Gln Glu Pro Gln Leu Ser Leu Gln Pro Glu Pro Val Phe Thr Val Asp Arg Ala Glu Val Pro Pro Leu Phe Trp Lys Pro Tyr Ile Tyr 25 20 Ala Gly Tyr Arg Pro Leu His Gln Thr Trp Arg Phe Tyr Phe Arg Thr 35 Leu Phe Gln Gln His Asn Glu Ala Val Asn Val Trp Thr His Leu Leu 55 Ala Ala Leu Val Leu Leu Arg Leu Ala Leu Phe Val Glu Thr Val 70 Asp Phe Trp Gly Asp Pro His Ala Leu Pro Leu Phe Ile Ile Val Leu 85 80 Ala Ser Phe Thr Tyr Leu Ser Leu Ser Ala Leu Ala His Leu Leu Gln 100 105 Ala Lys Ser Glu Phe Trp His Tyr Ser Phe Phe Phe Leu Asp Tyr Val 120 115 Gly Val Ala Val Tyr Gln Phe Gly Ser Ala Leu Ala His Phe Tyr Tyr 140 135 130 Ala Ile Glu Pro Ala Trp His Ala Gln Val Gln Ala Val Phe Leu Pro 150 Met Ala Ala Phe Leu Ala Trp Leu Ser Cys Ile Gly Ser Cys Tyr Asn 170 165 Lys Tyr Ile Gln Lys Pro Gly Leu Leu Gly Arg Thr Cys Gln Glu Val 185 180 Pro Ser Val Leu Ala Tyr Ala Leu Asp Ile Ser Pro Val Val His Arg 200 195 Ile Phe Val Ser Ser Asp Pro Thr Thr Asp Asp Pro Ala Leu Leu Tyr 215 210 His Lys Cys Gln Val Val Phe Phe Leu Leu Ala Ala Phe Phe Ser 230 225 Thr Phe Met Pro Glu Arg Trp Phe Pro Gly Ser Cys His Val Phe Gly 245 240 Gln Gly His Gln Leu Phe His Ile Phe Leu Val Leu Cys Thr Leu Ala 265 260 Gln Leu Glu Ala Val Ala Leu Asp Tyr Glu Ala Arg Arg Pro Ile Tyr

```
275
                                      280
 Glu Pro Leu His Thr His Trp Pro His Asn Phe Ser Gly Leu Phe Leu
                          295
               290
 Leu Thr Val Gly Ser Ser Ile Leu Thr Ala Phe Leu Leu Ser Gln Leu
           305
                            310
 Val Gln Arg Lys Leu Asp Gln Lys Thr Lys
        320
                           325
<210> 223
<211> 210
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
Met Asp Asn Arg Phe Ala Thr Ala Phe Val Ile Ala Cys Val Leu Ser
                   -15
                                       -10
Leu Ile Ser Thr Ile Tyr Met Ala Ala Ser Ile Gly Thr Asp Phe Trp
                              5
                                                 10
Tyr Glu Tyr Arg Ser Pro Val Gln Glu Asn Ser Ser Asp Leu Asn Lys
                           20
Ser Ile Trp Asp Glu Phe Ile Ser Asp Glu Ala Asp Glu Lys Thr Tyr
                       35
Asn Asp Ala Leu Phe Arg Tyr Asn Gly Thr Val Gly Leu Trp Arg Arg
                   5.0
                                       55
Cys Ile Thr Ile Pro Lys Asn Met His Trp Tyr Ser Pro Pro Glu Arg
               65
                                  70
Thr Glu Ser Phe Asp Val Val Thr Lys Cys Val Ser Phe Thr Leu Thr
                                               90
           80
                              85
Glu Gln Phe Met Glu Lys Phe Val Asp Pro Gly Asn His Asn Ser Gly
                          100
       95
                                            105
 Ile Asp Leu Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu Leu Pro
    110
                       115
                                         120
Phe Val Ser Leu Gly Leu Met Cys Phe Gly Ala Leu Ile Gly Leu Cys
125
                    130
                                       135
Ala Cys Ile Cys Arg Ser Leu Tyr Pro Thr Ile Ala Thr Gly Ile Leu
                                 150
                145
His Leu Leu Ala Val Thr Lys Glu Ser Met Leu Pro Ala Gly Ala Glu
                              165
                                                 170
            160
Ser Lys His Thr Ala Thr Pro Ala His Ala Cys Val Gln Thr Gly Lys
                           180
Pro Lys
   190
<210> 224
 <211> 184
 <212> PRT
```

```
<210> 224
<211> 184
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
```

<400> 224 .
Met Asp Asn Arg Phe Ala Thr Ala Phe Val Ile Ala Cys Val Leu Ser

```
-15
                                     -10
Leu Ile Ser Thr Ile Tyr Met Ala Ala Ser Ile Gly Thr Asp Phe Trp
Tyr Glu Tyr Arg Ser Pro Val Gln Glu Asn Ser Ser Asp Leu Asn Lys
                         20
Ser Ile Trp Asp Glu Phe Ile Ser Asp Glu Ala Asp Glu Lys Thr Tyr
                   35
Asn Asp Ala Pro Phe Arg Tyr Asn Gly Thr Val Gly Leu Trp Arg Arg
        50
Cys Ile Thr Ile Pro Lys Asn Met His Trp Tyr Ser Pro Pro Glu Arg
              65
                                  70
Thr Glu Ser Phe Asp Val Val Thr Lys Cys Val Ser Phe Thr Leu Thr
                              85
Glu Gln Phe Met Glu Lys Phe Val Asp Pro Gly Asn His Asn Ser Gly
                         100
Ile Asp Leu Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu Leu Pro
                     115
                                        120
Phe Val Ser Leu Gly Leu Met Cys Phe Gly Ala Leu Ile Gly Leu Cys
                 130
                                    135
Ala Cys Ile Cys Arg Ser Leu Tyr Pro Thr Ile Ala Thr Gly Ile Leu
              145
                       150
His Leu Leu Ala Asp Thr Met Leu
```

<210> 225 <211> 227 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -22..-1

<400> 225 Met Gly Trp Thr Met Arg Leu Val Thr Ala Ala Leu Leu Cly Leu -20 -15 -10 Met Met Val Val Thr Gly Asp Glu Asp Glu Asn Ser Pro Cys Ala His Glu Ala Leu Leu Asp Glu Asp Thr Leu Phe Cys Gln Gly Leu Glu Val 20 Phe Tyr Pro Glu Leu Gly Asn Ile Gly Cys Lys Val Val Pro Asp Cys 35 Asn Asn Tyr Arg Gln Lys Ile Thr Ser Trp Met Glu Pro Ile Val Lys 50 45 Phe Pro Gly Ala Val Asp Gly Ala Thr Tyr Ile Leu Val Met Val Asp 65 Pro Asp Ala Pro Ser Arg Ala Glu Pro Arg Gln Arg Phe Trp Arg His 80 Trp Leu Val Thr Asp Ile Lys Gly Ala Asp Leu Lys Lys Gly Lys Ile 100 Gln Gly Gln Glu Leu Ser Ala Tyr Gln Ala Pro Ser Pro Pro Ala His 115 Ser Gly Phe His Arg Tyr Gln Phe Phe Val Tyr Leu Gln Glu Gly Lys 130 Val Ile Ser Leu Leu Pro Lys Glu Asn Lys Thr Arg Gly Ser Trp Lys 145 150 Met Asp Arg Phe Leu Asn Arg Phe His Leu Gly Glu Pro Glu Ala Ser 160 165

Thr Gln Phe Met Thr Gln Asn Tyr Gln Asp Ser Pro Thr Leu Gln Ala 175 180 185

<210> 226 <211> 74 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -41..-1

<400> 226

<210> 227 <211> 73 <212> PRT <213> Homo sapiens

<210> 228
<211> 82
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1

<400> 228
Met Lys Arg Leu Leu Pro Ala Thr Ser Leu Ala Gly Pro Val Leu Ser
-15
Thr Leu Ile Ala Pro Thr Pro Met Leu Phe Cys Glu Asp Lys Ser Trp

چ: د ج

<210> 229 <211> 119 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL

<222> -56..-1

<400> 229 Met Ala Glu Pro Ser Ala Ala Thr Gln Ser His Ser Ile Ser Ser Ser -45 -50 Ser Phe Gly Ala Glu Pro Ser Ala Pro Gly Gly Gly Ser Pro Gly -30 -35 Ala Cys Pro Ala Leu Gly Thr Lys Ser Cys Ser Ser Ser Cys Ala Asp -15 -20 Ser Phe Val Ser Ser Ser Ser Gln Rrg Val Ser Leu Phe Ser Thr 1 -5 Ser Gln Glu Gly Leu Ser Ser Leu Cys Ser Asp Glu Pro Ser Ser Glu 15 Ile Met Thr Ser Ser Phe Leu Ser Ser Glu Ile His Asn Thr Gly 35 30 Leu Thr Ile Leu His Gly Glu Lys Ser His Val Leu Gly Ser Gln Pro 50 Ile Leu Ala Lys Lys Lys Lys 60

<210> 230 <211> 54 <212> PRT <213> Homo sapiens

<210> 231 <211> 210 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -14..-1
<400> 231
Met Leu Thr Leu Leu Gly Leu Ser Phe Ile Leu Ala Gly Leu Ile Val
               -10
                                   - 5
Gly Gly Ala Cys Ile Tyr Lys Tyr Phe Met Pro Lys Ser Thr Ile Tyr
                          10
Arg Gly Glu Met Cys Phe Phe Asp Ser Glu Asp Pro Ala Asn Ser Leu
Arg Gly Glu Pro Asn Phe Leu Pro Val Thr Glu Glu Ala Asp Ile
35
                 40
Arg Glu Asp Asp Asn Ile Ala Ile Ile Asp Val Pro Val Pro Ser Phe
                                   60
Ser Asp Ser Asp Pro Ala Ala Ile Ile His Asp Phe Glu Lys Gly Met
Thr Ala Tyr Leu Asp Leu Leu Gly Ile Cys Tyr Leu Met Pro Leu
                           90
                                              95
Asn Thr Ser Ile Val Met Pro Pro Lys Asn Leu Val Glu Leu Phe Gly
                      105
                                          110
Lys Leu Ala Ser Gly Arg Tyr Leu Pro Gln Thr Tyr Val Val Arg Glu
                   120
                                      125
Asp Leu Val Ala Val Glu Glu Ile Arg Asp Val Ser Asn Leu Gly Ile
               135
                                   140
Phe Ile Tyr Gln Leu Cys Asn Asn Arg Lys Ser Phe Arg Leu Arg Arg
           150
                               155
Arg Asp Leu Leu Cly Phe Asn Lys Arg Ala Ile Asp Lys Cys Trp
                        170
                                              175
Lys Ile Arg His Phe Pro Asn Glu Phe Ile Val Glu Thr Lys Ile Cys
                      185
                                          190
Gln Glu
195
```

<210> 232 <211> 108 <212> PRT <213> Homo sapiens

Leu Pro Glu Glu Pro Lys Gly Thr Gln Met Leu Thr 100 105

<210> 233 <211> 43

. .

```
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
<400> 233
Met Ser Ser Gly Arg Leu Arg Trp Leu Met Pro Val Ile Pro Ala Leu
                    -10
Trp Gly Ala Glu Lys Gly Glu Ser Pro Glu Val Ser Ser Phe Glu Thr
                   5
Arg Leu Ala Asn Met Ala Lys Pro Cys Leu Tyr
    20
<210> 234
<211> 36
<212> PRT
<213> Homo sapiens
<400> 234
Met Ser Ala Arg Ile Pro Phe Tyr Lys Asp Thr Ser Gln Ile Arg Leu
                                 10
Gly Ser Thr Ile Ile Pro His Phe Asn Leu Ile Thr Phe Val Lys Thr
          20
                             25
Phe Phe Gln Ile
 35
<210> 235
<211> 307
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -13..-1
<400> 235
Met Leu Ala Val Ser Leu Thr Val Pro Leu Leu Gly Ala Met Met Leu
     -10
                              - 5
Leu Glu Ser Pro Ile Asp Pro Gln Pro Leu Ser Phe Lys Glu Pro Pro
                      10
                                          15
Leu Leu Gly Val Leu His Pro Asn Thr Lys Leu Arg Gln Ala Glu
                  25
                                     30
Arg Leu Phe Glu Asn Gln Leu Val Gly Pro Glu Ser Ile Ala His Ile
                                  45
Gly Asp Val Met Phe Thr Gly Thr Ala Asp Gly Arg Val Val Lys Leu
                              60
Glu Asn Gly Glu Ile Glu Thr Ile Ala Arg Phe Gly Ser Gly Pro Cys
                          75
Lys Thr Arg Asp Asp Glu Pro Val Cys Gly Arg Pro Leu Gly Ile Arg
                       90
Ala Gly Pro Asn Gly Thr Leu Phe Val Ala Asp Ala Cys Lys Gly Leu
                  105
                                      110
Phe Glu Val Asn Pro Trp Lys Arg Glu Val Lys Leu Leu Ser Ser
                                 125
               120
Glu Thr Pro Ile Glu Gly Lys Asn Met Ser Phe Val Asn Asp Leu Thr
          135
                              140
```

Val Ser Gln Asp Gly Arg Lys Ile Tyr Phe Thr Asp Ser Ser Ser Lys 155 160 Trp Gln Arg Arg Asp Tyr Leu Leu Leu Val Met Glu Gly Thr Asp Asp 170 175 Gly Arg Leu Leu Glu Tyr Asp Thr Val Thr Arg Glu Val Lys Val Leu 185 190 Leu Asp Gln Leu Arg Phe Pro Asn Gly Val Gln Leu Ser Pro Ala Glu 200 205 Asp Phe Val Leu Val Ala Glu Thr Thr Met Ala Arg Ile Arg Arg Val 215 220 Tyr Val Ser Gly Leu Met Lys Gly Gly Ala Asp Leu Phe Val Glu Asn 235 240 Met Pro Gly Phe Pro Asp Asn Ile Arg Pro Ser Ser Ser Gly Gly Tyr 250 255 Trp Val Gly Met Ser Thr Ile Arg Pro Asn Pro Gly Phe Ser Met Leu 265 270 Asp Phe Leu Ser Glu Arg Pro Trp Ile Lys Arg Met Ile Phe Lys Ala 285 Lys Lys Lys

<210> 236 <211> 106 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -32..-1

<400> 236 Met Phe Ala Pro Ala Val Met Arg Ala Phe Arg Lys Asn Lys Thr Leu -25 -20 Gly Tyr Gly Val Pro Met Leu Leu Leu Ile Val Gly Gly Ser Phe Gly -15 -10 Leu Arg Glu Phe Ser Gln Ile Arg Tyr Asp Ala Val Lys Ser Lys Met 5 10 Asp Pro Glu Leu Glu Lys Lys Leu Lys Glu Asn Lys Ile Ser Leu Glu 20 25 Ser Glu Tyr Glu Lys Ile Lys Asp Ser Lys Phe Asp Asp Trp Lys Asn 3.5 40 45 Ile Arg Gly Pro Arg Pro Trp Glu Asp Pro Asp Leu Leu Gln Gly Arg 55 Asn Pro Glu Ser Leu Lys Thr Lys Thr Thr 70

<210> 237 <211> 42 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> 237

Met Asp Leu Arg Gln Phe Leu Met Cys Leu Ser Leu Cys Thr Ala Phe -15 -10 -5 Ala Leu Ser Lys Pro Thr Glu Lys Lys Asp Arg Val His His Glu Pro

WO 99/31236 -163- PCT/IB98/02122

```
10
Gln Leu Ser Asp Lys Val His Asn Asp Ile
                       20
<210> 238
<211> 117
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 238
Met Asp Asn Arg Phe Ala Thr Ala Phe Val Ile Ala Cys Val Leu Ser
                  -15
                                      -10
Leu Ile Ser Thr Ile Tyr Met Ala Ala Ser Ile Gly Thr Asp Phe Trp
                            5
            1
Tyr Glu Tyr Arg Ser Pro Val Gln Glu Asn Ser Ser Asp Leu Asn Lys
                           20
                                             25
Ser Ile Trp Asp Glu Phe Ile Ser Asp Glu Ala Asp Glu Lys Thr Tyr
                     35
Asn Asp Ala Leu Phe Arg Tyr Asn Gly Thr Val Gly Leu Trp Gly Arg
                50
                                   . . 55
Cys Ile Thr Ile Pro Lys Asn Met His Trp Tyr Ser Pro Pro Glu Arg
               65
                                 70
Thr Gly Ile Ser Leu Ile Leu Thr Ser Val Phe Phe Thr Trp Leu Ile
                              85
Ile Asp Lys Thr Thr
      95
<210> 239
<211> 178
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
<400> 239
Met Glu Arg Gln Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe
      -35
                           -30
                                              - 25
Gln His Xaa Xaa Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile
                       -15
                                          -10
Leu Thr Ile Leu Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe
Leu His Glu Thr Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu
                               20
Ile Ser Arg Tyr Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val
    30
                           35
Cys Asp Cys Val Lys Leu Thr Phe Ser Pro Pro Thr Leu Leu Val Asn
  45
                       50
Val Thr Asp Gln Val Tyr Glu Tyr Lys Tyr Lys Arg Glu Ile Ser Gln
                   65
                                      70
His Asn Ile Asn Pro His Gln Gly Asn Ala Ile Leu Glu Lys Met Thr
```

85

Phe Asp Pro Glu Ile Phe Phe Asn Val Leu Leu Pro Pro Ile Ile Phe

```
100
His Ala Gly Tyr Ser Leu Lys Lys Arg His Phe Phe Gln Asn Leu Gly
               115
       110
                                            120
Ser Ile Leu Thr Tyr Ala Phe Leu Gly Thr Ala Ile Ser Cys Ile Val
                      130
                                         135
Ile Gly
140
<210> 240
<211> 126
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27...-1
<400> 240
Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly Val Val
    -25
                          -20
Val Leu Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr Glu Ser
   -10
                      ~ 5
Met Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Ile Phe Ile
                                 15
Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr Met Ala
          25
                             30
                                                35
Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys Asp Tyr
       40
                          45
Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met Lys Gly
                      60
Leu Lys Cys Arg Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro
                   75
                                     80
Tyr Phe Lys Met His Lys Pro Val Thr Met Lys Lys Lys
               90
<210> 241
<211> 174
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -115..-1
<400> 241
Met Arg Trp Ser Cys Glu His Leu Val Met Val Trp Ile Asn Ala Phe
-115 -110
                        -105
Val Met Leu Thr Thr Gln Leu Leu Pro Ser Lys Tyr Cys Asp Leu Leu
                                  - 90
               -95
His Lys Ser Ala Ala His Leu Gly Lys Trp Gln Lys Leu Glu His Gly
          -80
                              -75
                                                 - 70
```

Ser Tyr Ser Asn Ala Pro Gln His Ile Trp Ser Glu Asn Thr Ile Trp

Gly Pro Tyr Asn Val Ala Val Pro Ser Asp Val Ser His Ala Arg Phe

Tyr Phe Leu Phe His Arg Pro Leu Arg Leu Leu Asn Leu Leu Ile Leu

- 2 5

-60 Pro Gln Gly Val Leu Val Arg His Ser Arg Cys Leu Tyr Arg Ala Met

-45

-30

-65

-35

- 55

-40

-15

Ile Glu Gly Gly Val Val Phe Tyr Gln Leu Tyr Ser Leu Leu Arg Ser 5 10 Glu Lys Trp Asn His Thr Leu Ser Met Ala Leu Ile Leu Phe Cys Asn 20 25 Tyr Tyr Val Leu Phe Lys Leu Leu Arg Asp Arg Ile Val Leu Gly Arg 35 40 Ala Tyr Ser Tyr Pro Leu Asn Ser Tyr Glu Leu Lys Ala Asn 50 55 <210> 242 <211> 896 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18..173 <221> sig_peptide <222> 18..77 <223> Von Heijne matrix score 6.5 seq GLCVLQLTTAVTS/AF <221> polyA_signal <222> 864..869 <221> polyA site <222> 882..893 <400> 242 50 aaccttcaca gtgtgag atg cct agt gtg aac agt gct gga tta tgt gtc Met Pro Ser Val Asn Ser Ala Gly Leu Cys Val -20 -15 ttg cag ttg aca acg gca gtr acc agt gcc ttt tta cta gca aaa gtg 98 Leu Gln Leu Thr Thr Ala Val Thr Ser Ala Phe Leu Leu Ala Lys Val -5 146 aat cot tto gaa rot ttt oto toa agg ggo ttt tgg ota tgt got goo Asn Pro Phe Glu Xaa Phe Leu Ser Arg Gly Phe Trp Leu Cys Ala Ala 10 15 cat cat ttc att cat cct tgc ctg gat tgagacgtgt tcctgattca 193 His His Phe Ile His Pro Cys Leu Asp aagtgttacc tcaagaagca gaagaagaaa acagactcct gatagttcag gatgcttcag 253 313 agagggcage acttatacet ggtggtettt etgatggtea gttttattee eeteetgaat 373 ccgaagcagg atctgaagaa gctgaagaaa aacaggacag tgagaaacca cttttagaac 433 tatgagtact actitigtta aatgigaaaa accetcacag aaagicateg aggcaaaaag 493 aggcaggcag tggagtctcc ctgtcgacag taaagttgaa atggtgacgt ccactgctgg ctttattgaa cagctaataa agatttattt attgtaatac ctcacagacg ttgtaccata tccatgcaca tttagttgcc tgcctgtggc tggtaaggta atgtcatgat tcatcctctc ttcagtgaga ctgagcctga tgtgttaaca aataggtgaa gaaagtcttg tgctgtattc 673 ctaatcaaaa gacttaatat attgaagtaa cactttttta gtaagcaaga taccttttta 733 793 tttcaattca cagaatqqaa tttttttgtt tcatgtctca gatttatttt gtatttcttt 853 tttaacactc tacatttccc ttgtttttta actcatgcac atgtgctctt tgtacagttt

896

taaaaagtgt aataaaatct gacatgtcaa araaaaaaaa mcy

```
<211> 851
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 17..595
<221> sig_peptide
<222> 17..85
<223> Von Heijne matrix
      score 3.70000004768372
      seq FLPPLXRAFACRG/CQ
<221> polyA signal
<222> 820..825
<221> polyA_site
<222> 840..851
<400> 243
aagggggegt ggggcc atg gtg gtc ttg cgg gcg ggg aag aag acc ttt ctc
                  Met Val Val Leu Arg Ala Gly Lys Lys Thr Phe Leu
                              -20
                                                  -15
ccc cct ctm wgc cgc gcc ttc gcc tgc cgc ggc tgt caa ctc gct ccg
                                                                     100
Pro Pro Leu Xaa Arg Ala Phe Ala Cys Arg Gly Cys Gln Leu Ala Pro
    -10
                        - 5
gag ege gge gee gag ege agg gat aca geg eee age ggg gte tea aga
                                                                      148
Glu Arg Gly Ala Glu Arg Arg Asp Thr Ala Pro Ser Gly Val Ser Arg
                10
                                    15
ttc tgc cct cca aga aag tct tgc cat gat tgg ata gga ccc cca gat
                                                                      196
Phe Cys Pro Pro Arg Lys Ser Cys His Asp Trp Ile Gly Pro Pro Asp
                                30
aaa tat toa aac ott oga oot gtt oac ttt tac ata oot gaa aat gaa
                                                                      244
Lys Tyr Ser Asn Leu Arg Pro Val His Phe Tyr Ile Pro Glu Asn Glu
                            45
                                                50
                                                                      292
tot coa tig gaa caa aag ott aga aaa tia aga caa gaa aca caa gaa
Ser Pro Leu Glu Gln Lys Leu Arg Lys Leu Arg Gln Glu Thr Gln Glu
                        60
                                                                      340
tgg aat caa cag ttc tgg gca aac cag aat ttg act ttt agt aag gaa
Trp Asn Gln Gln Phe Trp Ala Asn Gln Asn Leu Thr Phe Ser Lys Glu
70
                    75
                                        80
aaa gaa gaa ttt att cac tca aga cta aaa act aaa ggc ctg ggc ctg
                                                                      388
Lys Glu Glu Phe Ile His Ser Arg Leu Lys Thr Lys Gly Leu Gly Leu
                90
                                    95
aga act gaa toa ggt cag aaa gca aca ttg aat gca gaa gaa atg gcg
                                                                      436
Arg Thr Glu Ser Gly Gln Lys Ala Thr Leu Asn Ala Glu Glu Met Ala
                                110
                                                                      484
gac ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cac atg tat
Asp Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys His Met Tyr
        120
                            125
                                                130
                                                                      532
tat aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg
Tyr Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met
                        140
                                            145
gga aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa
                                                                      580
Gly Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln
                    155
                                         160
                                                                      635
aag aag agg agc aac taggagteca etetgaecca gecagagtec aggtttecae
Lys Lys Arg Ser Asn
aggaagcara tggagctcct ttcacagggg ctctgagaaa aactggagct gatctcaaga
agenceacat cttcctaagg ggccccatgg cctgtttggg ggcagggtag gtcctggggc
```

gtgaaa	taaa	gccc	aagca	ac to	gggaa	aaaa	tci aaa	aggo	cag	cttg	jttgt	ca d	egtad	gtggt	815 851
<210><211><212><213>	495 DNA	sapie	ens												
<220>		-					,						•		
<221> <222>		34					•	•							
<221> <222>			ie .				· entre	<b>₽</b>							
<223>		eijne 3.59	9999	99046		7	:	;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;							
<221> )			nal					<b>ب</b>							
<221>   <222> (		-	•					-							
<400>	244			•				٠.,							
agtagg: ttggac	aasg (	333c	gect	gt gg	gaggo	gcc a	tg g	gcc t	itt a	cc c	tg t	as	gagan tca d Ser I	etg	60 112
ctg cag	ttcg (	gcc 9 <b>gg</b> c9	geet	ctc	gacgo tgc	gcc a M gtc	let 7	gcc t	tt a Phe T atc	icc of the land of	tg t Leu 2 ·10 gtg	tas ( Kaa : ctg	tca d Ser I cac	etg Leu gag	
ctg cag Leu Gli	g gca n Ala	gggcg gcc Ala	gcct ctg Leu	ctc Leu	tgc Cys	gcc a M gtc Val	let i aac Asn	gcc Ala	tt a he T atc Ile 5	ncc of thr I gca Ala	tg t Leu X 10 gtg Val	tas Kaa Ctg Leu	cac His	gag Glu	112
ctg cag Leu Gli	g gca n Ala a ttc	gcc Ala ctc	ctg Leu aag Lys	ctc Leu aac	tgc Cys 1	gtc Val ggc	et 7 aac Asn	gcc Ala gga Gly	atc Ile aca	gca Ala	tg teu 2 10 gtg Val	ctg Leu	cac His	gag Glu 10 ggt	112
ctg cag Leu Gli -5 gag cg Glu Arg	g gca n Ala a ttc g Phe	gcc Ala ctc Leu	ctg Leu aag Lys 15 gag	ctc Leu aac Asn	tgc Cys 1 att Ile	gtc Val ggc Gly	aac Asn tgg Trp	gcc Ala gga Gly 20 tca	atc Tle saca Thr	gca Ala gac Asp	tg teu ) -10 gtg Val cag Gln atg	ctg Leu gga Gly	cac His att Ile 25	gag Glu 10 ggt Gly	112
ctg cag Leu Gli -5 gag cg Glu Arg gga tt Gly Pho	g gca n Ala a ttc g Phe t gga e Gly	gcc Ala ctc Leu gaa Glu 30	ctg Leu aag Lys 15 gag Glu	ctc Leu aac Asn ccg Pro	tgc Cys 1 att Ile gga Gly	gtc Val ggc Gly att Ile	aac Asn tgg Trp aaa Lys 35	gcc Ala gga Gly 20 tca Ser	atc Ile 5 aca Thr sag	gca Ala gac Asp sta	tg tell (10 gtg Val cag Gln atg Met	ctg Leu gga Gly avs Xaa	cac His att Ile 25 ctt Leu	gag Glu 10 ggt Gly att	112 160 208 256
ctg cag Leu Gli -5 gag cg Glu Arg	g gca n Ala a ttc g Phe t gga e Gly	gcc Ala ctc Leu gaa Glu 30	ctg Leu aag Lys 15 gag Glu	ctc Leu aac Asn ccg Pro	tgc Cys 1 att Ile gga Gly	gtc Val ggc Gly att Ile aga	aac Asn tgg Trp aaa Lys 35 gtg	gcc Ala gga Gly 20 tca Ser	atc Ile Saca Thr sag Xaa	gca Ala gac Asp sta Xaa	tg tell (10 gtg Val cag Gln atg Met ata	ctg Leu gga Gly avs Xaa 40 gta	cac His att Ile 25 ctt Leu	gag Glu 10 ggt Gly att Ile	112 160 208
ctg cag Leu Gli -5 gag cg Glu Ard gga tt Gly Pho cga tc Arg Se att gc Ile Al	g gcan Ala ttcg Phe t gga e Gly tal 45 a att	gcc Ala ctc Leu gaa Glu 30 aga Arg	ctg Leu aag Lys 15 gag Glu acc Thr	ctc de ctc Leu aac Asn ccg Pro gtg Val	tgc Cys 1 att Ile gga Gly atg Met tta Leu	gcc a M gtc Val ggc Gly att Ile aga Arg 50 tta	aac Asn tgg Trp aaa Lys 35 gtg Val	gcc Ala gga gga gga ser cca pro	atc Ile Saca Thr sag Xaa ttg Leu	gca Ala gac Asp sta Xaa ata Ile	tg teu ) 10 gtg Val cag Gln atg Met ata Ile 55	ctg Leu gga Gly avs Xaa 40 gta Val	cac His att Ile 25 ctt Leu aac Asn	gag Glu 10 ggt Gly att Ile tca Ser	112 160 208 256
ctg cag Leu Gli -5 gag cg Glu Ard gga tt Gly Pho cga tc Arg Se att gc Ile Ali 60 ggakac	g gcan Ala attcg Phe c gga r Val 45 a att a Ile	gcc Ala ctc Leu gaa Glu 30 aga Arg Val	ctg Leu aag Lys 15 gag Glu acc Thr tta Leu	ctc Leu aac Asn ccg Pro gtg Val ctt Leu	tgc Cys 1 att Ile gga Gly atg Met tta Leu 65 ccakt	gtc Val ggc Gly att Ile aga Arg 50 tta Leu	aac Asn tgg Trp aaa Lys 35 gtg Val ttt Phe	gcc Ala gcc Ala gga Gly 20 tca Ser cca Pro gga Gly	atc Ile Saca Thr sag Xaa ttg Leu tgaa	gca Ala gac Asp sta Xaa ata Ile	etg ( eu ) 10 gtg Val cag Gln atg Met ata Ile 55	ctg Leu gga Gly avs Xaa 40 gta Val	cac His att Ile 25 ctt Leu aac Asn gaaaa	gag Glu 10 ggt Gly att Ile tca Ser at	112 160 208 256 304 354
ctg cag Leu Gli -5 gag cg Glu Ard gga tt Gly Pho cga tc Arg Se att gc Ile Al	g gcan Ala ttc g Phe t gga r Val 45 a att a Ile	gcc Ala ctc Leu gaa Glu 30 aga Arg Val	ctg Leu aag Lys 15 gag Glu acc Thr tta Leu	ctc Leu aac Asn ccg Pro ytg Val ctt Leu	tgc Cys 1 att Ile gga Gly atg Met tta Leu 65 ccakt	gtc Val ggc Gly att Ile aga Arg 50 tta Leu	aac Asn tgg Trp aaa Lys 35 gtg Val ttt Phe	gcc Ala gcc Ala gga Gly 20 tca Ser cca Pro gga Gly	atc Ile Saca Thr sag Xaa ttg Leu tgaa	gca Ala gac Asp sta Xaa ata Ile	etg ( eu ) 10 gtg Val cag Gln atg Met ata Ile 55	ctg Leu gga Gly avs Xaa 40 gta Val	cac His att Ile 25 ctt Leu aac Asn gaaaa	gag Glu 10 ggt Gly att Ile tca Ser at	112 160 208 256 304 354
ctg cag Leu Gli -5 gag cg Glu Ard gga tt Gly Pho cga tc Arg Se att gc Ile Ala 60 ggakac atatct	g gcan Ala ttc g Phe t gga r Val 45 a att a Ile	gcc Ala ctc Leu gaa Glu 30 aga Arg Val	ctg Leu aag Lys 15 gag Glu acc Thr tta Leu	ctc Leu aac Asn ccg Pro ytg Val ctt Leu	tgc Cys 1 att Ile gga Gly atg Met tta Leu 65 ccakt	gtc Val ggc Gly att Ile aga Arg 50 tta Leu	aac Asn tgg Trp aaa Lys 35 gtg Val ttt Phe	gcc Ala gcc Ala gga Gly 20 tca Ser cca Pro gga Gly	atc Ile Saca Thr sag Xaa ttg Leu tgaa	gca Ala gac Asp sta Xaa ata Ile	etg ( eu ) 10 gtg Val cag Gln atg Met ata Ile 55	ctg Leu gga Gly avs Xaa 40 gta Val	cac His att Ile 25 ctt Leu aac Asn gaaaa	gag Glu 10 ggt Gly att Ile tca Ser at	112 160 208 256 304 354 414 474
ctg cag Leu Gli -5 gag cg Glu Ard gga tt Gly Pho cga tc Arg Se att gc Ile Ala 60 ggakac atatct	g gcan Ala attc g Phe c gga r Val 45 a att a Ile tcag c ttta	gcc Ala ctc Leu gaa Glu 30 aga Arg Val	ctg Leu aag Lys 15 gag Glu acc Thr tta Leu	ctc Leu aac Asn ccg Pro ytg Val ctt Leu	tgc Cys 1 att Ile gga Gly atg Met tta Leu 65 ccakt	gtc Val ggc Gly att Ile aga Arg 50 tta Leu	aac Asn tgg Trp aaa Lys 35 gtg Val ttt Phe	gcc Ala gcc Ala gga Gly 20 tca Ser cca Pro gga Gly	atc Ile Saca Thr sag Xaa ttg Leu tgaa	gca Ala gac Asp sta Xaa ata Ile	etg ( eu ) 10 gtg Val cag Gln atg Met ata Ile 55	ctg Leu gga Gly avs Xaa 40 gta Val	cac His att Ile 25 ctt Leu aac Asn gaaaa	gag Glu 10 ggt Gly att Ile tca Ser at	112 160 208 256 304 354 414 474

<222> 21..83 <223> Von Heijne matrix score 10 seq LWALAMVTRPASA/AP <221> polyA_signal <222> 849..854 <221> polyA site <222> 873..884 <400> 245 aatacettag acceteagte atg cea gtg cet get etg tge etg etc tgg gee 53 Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala -20 -15 ctg gca atg gtg acc cgg cct gcc tca gcg gcc ccc atg ggc ggc cca 101 Leu Ala Met Val Thr Arg Pro Ala Ser Ala Ala Pro Met Gly Gly Pro -10 - 5 1 gaa ctg gca cag cat gag gag ctg acc ctg ctc ttc cat ggg acc ctg 149 Glu Leu Ala Gln His Glu Glu Leu Thr Leu Leu Phe His Gly Thr Leu 10 15 20 cag ctg ggc cag gcc ctc aac ggt gtg tac agg acc acg gag gga egg 197 Gln Leu Gly Gln Ala Leu Asn Gly Val Tyr Arg Thr Thr Glu Gly Arg 30 35 ctg aca aag gcc agg aac agc ctg ggt ctc tat ggc cgc aca ata gaa 245 Leu Thr Lys Ala Arg Asn Ser Leu Gly Leu Tyr Gly Arg Thr Ile Glu 40 45 ctc ctg ggg cag gag gtc agc cgg ggc cgg gat gca gcc cag gaa ctt 293 Leu Leu Gly Gln Glu Val Ser Arg Gly Arg Asp Ala Ala Gln Glu Leu 60 65 cgg gca agc ctg ttg gaa act car atg gag gag gat att ctg cas ctg 341 Arg Ala Ser Leu Leu Glu Thr Gln Met Glu Glu Asp Ile Leu Xaa Leu 80 cag gca rag gcc aca gct gag gtg ctg ggg gag gtg gcc cag gca car 389 Gln Ala Xaa Ala Thr Ala Glu Val Leu Gly Glu Val Ala Gln Ala Gln 90 95 aag gtg cta cgg gac agc gtg cag cgg cta daa ktc cag ctg arg asc 437 Lys Val Leu Arg Asp Ser Val Gln Arg Leu Xaa Xaa Gln Leu Xaa Xaa 110 115 gcc tgg ctg ggc cct gcc tac cga aaa ttt gar gtc tta aag gcy ccc 485 Ala Trp Leu Gly Pro Ala Tyr Arg Lys Phe Glu Val Leu Lys Ala Pro 125 130 cck gam aar car aac cac atc cta tgg gcc ctc aca ggc cac gtg cak 533 Pro Xaa Lys Gln Asn His Ile Leu Trp Ala Leu Thr Gly His Val Xaa 140 145 cgg car arg cgg gar atg gtg gca cag cag cwt ckg ctg cna car atc 581 Arg Gln Xaa Arg Glu Met Val Ala Gln Gln Xaa Xaa Leu Xaa Gln Ile 155 160 165 cag gar aaa ctc cac aca gcg gcg ctc cca gcc tgaatctgcc tggatggaac 634 Gln Glu Lys Leu His Thr Ala Ala Leu Pro Ala 170 175 tgaggaccaa tcatgctgca aggaacactt ccacgccccg tgaggcccct gtgcagggag 694 gagetgeetg tteaetggga teageeaggg egeegggeee caettetgag caeagagear 754 agacagacgc aggcggggac aaaggcagag gatgtagccc cattgggggag gggtggagga 814 aggacatgta ccctttcatr mctacacacc cctcattaaa gcavagtcgt ggcatctcaa 874 aaaaaaaaa 884

<210> 246

<211> 897

<212 > DNA

```
<213> Homo sapiens
<220>
<221> CDS
<222> 94..573
<221> sig_peptide
<222> 94..258
<223> Von Heijne matrix
      score 4.69999980926514
      seq IGILCSLLGTVLL/WV
<221> polyA signal
<222> 862..867
<221> polyA_site
<222> 886..897
<400> 246
aagggcggct gcctagcacc cggaagagcc gtcaacttag cgagcgcaac aggctgccqc
                                                                     60
tgaggagctg gagctggtgg ggactgggcc gca atg gac aaq ctg aag aag gtg
                                     Met Asp Lys Leu Lys Lys Val
                                     -55
                                                         -50
ctg age ggg cag gac acg gag gac egg age gge etg tee gag gtt gtt
                                                                     162
Leu Ser Gly Gln Asp Thr Glu Asp Arg Ser Gly Leu Ser Glu Val Val
            -45
                                -40
                                                    -35
gag gca tot toa tta ago tgg agt acc agg ata aaa ggc tto att gcg
                                                                     210
Glu Ala Ser Ser Leu Ser Trp Ser Thr Arg Ile Lys Gly Phe Ile Ala
       -30
                           -25
                                               -20
tgt ttt gct ata gga att ctc tgc tca ctg ctg ggt act gtt ctg ctg
                                                                     258
Cys Phe Ala Ile Gly Ile Leu Cys Ser Leu Leu Gly Thr Val Leu Leu
                        -10
tgg gtg ccc agg aag gga cta cac ctc ttc gca gtg ttt tat acc ttt
                                                                     306
Trp Val Pro Arg Lys Gly Leu His Leu Phe Ala Val Phe Tyr Thr Phe
                                   10
ggt aat atc gca tca att ggg agt acc atc ttc ctc atg gga cca gtg
                                                                     354
Gly Asn Ile Ala Ser Ile Gly Ser Thr Ile Phe Leu Met Gly Pro Val
            20
                                25
aaa cag ctg aag cga atg ttt gag cct act cgt ttg att gca act atc
                                                                     402
Lys Gln Leu Lys Arg Met Phe Glu Pro Thr Arg Leu Ile Ala Thr Ile
                            40
                                               45
atg gtg ctg ttg tgt ttt gca ctt acc ctg tgt tct gcc ttt tgg tgg
                                                                     450
Met Val Leu Cys Phe Ala Leu Thr Leu Cys Ser Ala Phe Trp Trp
                       55
cat aac aag gga ctt gca ctt atc ttc tgc att ttg cag tct ttg gca
                                                                     498
His Asn Lys Gly Leu Ala Leu Ile Phe Cys Ile Leu Gln Ser Leu Ala
                    70
                                       75
ttg acg tgg tac agc ctt tcc ttc ata cca ttt gca agg gat gct gtg
                                                                      546
Leu Thr Trp Tyr Ser Leu Ser Phe Ile Pro Phe Ala Arg Asp Ala Val
                85
                                    90
aaa aad tgt ttt goo gtg tgt ott goa taattoatgg coagttttat
                                                                      593
Lys Xaa Cys Phe Ala Val Cys Leu Ala
            100
                                105
gaagetttgg aaggeactat ggacagaage tggtggacag ttttgtwact atettegaaa
                                                                      653
cototgtott acagacatgt goottttato ttgcagcaat gigtigottg tgattcgaac
                                                                      713
                                                                      773
atttgagggt tacttttgga agcaacaata cattctcgaa cctgaatgtc agtagcacag
gatgagaagt gggttctgta tcttgtggag tggaatcttc ctcatgtacc tgtttcctct
ctggatgttg tcccactgaa ttcccatgaa tacaaaccta ttcagcaaca gcaaaaaaaa
                                                                      897
```

```
<210> 247
<211> 518
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 74..397
<221> sig_peptide
<222> 74..127
<223> Von Heijne matrix
     score 7.69999980926514
     seq LLLLPVLGLLVSS/KT
<221> polyA_signal
<222> 472..477
<221> polyA_site
<222> 507..518
<400> 247
aaagaaagag ctgcsgtgca ggaattcgtg tgccggattt ggttagctga gcccaccgag
aggegeetge agg atg aaa get ete tgt ete ete ete eet gte etg
                                                                  109
              Met Lys Ala Leu Cys Leu Leu Leu Pro Val Leu
                         -15
                                            -10
ggg ctg ttg gtg tct agc aag acc ctg tgc tcc atg gaa gaa gcc atc
                                                                  157
Gly Leu Leu Val Ser Ser Lys Thr Leu Cys Ser Met Glu Glu Ala Ile
   -5
                       1
aat gag agg atc cag gag gtc gcc ggc tcc cta ata ttt agg gca ata
                                                                  205
Asn Glu Arg Ile Gln Glu Val Ala Gly Ser Leu Ile Phe Arg Ala Ile
               15
                                  20
age age att gge ega ggg age gag age gte ace tee agg ggg gae etg
                                                                  253
Ser Ser Ile Gly Arg Gly Ser Glu Ser Val Thr Ser Arg Gly Asp Leu
                                                  40
           30 .
                              35
                                                                  301
get act tgc ccc cga ggc ttc gcc gtc acc ggc tgc act tgt ggc tcc
Ala Thr Cys Pro Arg Gly Phe Ala Val Thr Gly Cys Thr Cys Gly Ser
                          50
       45
gcc tgt ggc tcg tgg gat gtg cgc gcc gag acc aca tgt cac tgc cag
                                                                  349
Ala Cys Gly Ser Trp Asp Val Arg Ala Glu Thr Thr Cys His Cys Gln
                       65
                                          70
                                                                  397
tgc gcg ggc atg gac tgg acc gga gcg cgc tgc tgt cgt gtg cag ccc
Cys Ala Gly Met Asp Trp Thr Gly Ala Arg Cys Cys Arg Val Gln Pro
                                      85
                  80
tgaggtcgcg cgcagcgcgt gcacagcgcg ggcggaggcg gctccaggtc cggaggggtt
                                                                  457
                                                                  517
518
```

```
<210> 248
```

<211> 350

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 51..242

<221> sig_peptide

<222> 51..116

<223> Von Heijne matrix

score 6.5 seq SCLCPALFPGTSS/FI <221> polyA_signal <222> 319..324 <221> polyA_site <222> 339..350 <400> 248 acgtcattcc aaaaccacac ccttgcaaag ctttgtactc cgcaccccag atg atc 56 Met Ile too agg cag etc aga tot oft too tgc oft tgc cot gca otg tto coc 104 Ser Arg Gln Leu Arg Ser Leu Ser Cys Leu Cys Pro Ala Leu Phe Pro -15 -10 ggt act tee tee ttt att gta gea ete age tee eea gee gat etg tae 152 Gly Thr Ser Ser Phe Ile Val Ala Leu Ser Ser Pro Ala Asp Leu Tyr 1 5 10 atc cct cav agg cas cga tct gat gaa ttg gtt ttt gaa tcc car aaa 200 Ile Pro Xaa Arg Xaa Arg Ser Asp Glu Leu Val Phe Glu Ser Gln Lys 20 ggg tot gcc atg gag ttg gca gtc atc acg gta rat ggc gta 242 Gly Ser Ala Met Glu Leu Ala Val Ile Thr Val Xaa Gly Val 35 40 tgattttgct gaattttaaa taaaatgaaa accataaatt acatratgct tttattgach 302 cttgacmact ggcctaaata aaaaractct gactccaaaa aaaaaaaa 350 <210> 249 <211> 996 <212> DNA <213> Homo sapiens <220> · <221> CDS <222> 111..191 <221> sig_peptide <222> 111..155 <223> Von Heijne matrix score 5.80000019073486 seg FLXLMTLTTHVHS/SA <221> polyA signal <222> 965..970 <221> polyA_site <222> 986..996 <400> 249 60 atcogataca gaacatgcag taatgtggac tgcccaccag aagcaggtga tttccgagct 116 cagcaatgct cagctcataa tgatgtcaag caccatggcc agttttatga atg ggy Met Gly 164 tto ctg wgt cta atg acc ctg aca acc cat gtt cac tca agt gcc aag Phe Leu Xaa Leu Met Thr Leu Thr Thr His Val His Ser Ser Ala Lys -10 - 5 211 cca aat gaa caa ccc tgg ttg ttg aac tagcacctaa ggtcttarat Pro Asn Glu Gln Pro Trp Leu Leu Asn

ggtacgcgtt gctatacaga atctttggat atgtgcatca gtggtttatg ccaaattgtt

271

WO 99/31236 -172-PCT/1B98/02122

ggctgcgatc accagctggg anatgggtcca cctgccggct ggtcctgatc acttatatct gacwdagaga tactgagaatt tagaggggata cggtgctgacag tggagggata cggattctt tcggctgag gctacgatct tacccagaga acatcaaacc gccaggtcag tcaaatttgc ttatttaaat taaaatgaaa aaaaa	ggtccgaggg cartataaat aattccctat ggaagtakac ggaarccawa accetccagg cettgtggac aattctagtg ggctggacca ctcacagcag tacagtccag kkcatettet teettgetca gcaacetgtg gaggagcaac cgtgtggttg caaacccaag ettcaggagt tagttcattt gtcataaaca	cccakctete egeaaccaaa 39 atattegeet tgtettaaaa 45 ggactaawgg tgaaaacagt 51 tggactteca gaawttteca 57 attteattgt caawattegt 63 atcaacccat catecaccga 69 gaggaggtta teagetgaca 75 etgaccaata etgteactat 81 gcaacttgga teettgteca 87 taactcaagt teeaaatagg 93	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
<210> 250 <211> 86C <212> DNA <213> Homo sapiens			
<220> <221> CDS <222> 45602	•		
<221> sig_peptide <222> 45107 <223> Von Heijne matrix score 8.5 seq LLTIVGLILPTRO			
<221> polyA_signal <222> 828833	·		
<221> polyA_site <222> 850860			
<400> 250 acctctctcc acgaggetge o	eggettagga eccecagete	cgac atg tcg ccc tct 50 Met Ser Pro Ser -20	6
ggt cgc ctg tgt ctt ctc Gly Arg Leu Cys Leu Leu -15	acc atc gtt ggc ctg Thr Ile Val Gly Leu -10	att ctc ccc acc aga 10- Ile Leu Pro Thr Arg	4
gga cag acg ttg aaa gat Gly Gln Thr Leu Lys Asp 1 5			2
atc atg gac att cag gtc Ile Met Asp Ile Gln Val	c ccg aca cga gcc cca l Pro Thr Arg Ala Pro 25	gat gca gtc tac aca 20 Asp Ala Val Tyr Thr 30	0
gaa ctc cag ccc acc tct Glu Leu Gln Pro Thr Ser 35	Pro Thr Pro Thr Trp	Pro Ala Asp Glu Thr 45	8
cca caa ccc cag acc cag Pro Gln Pro Gln Thr Gln 50	Thr Gln Gln Leu Glu 55	Gly Thr Asp Gly Pro 60	6
cta gtg aca gat cca gag Leu Val Thr Asp Pro Glu 65	Thr His Xaa Ser Xaa 70	Lys Ala Ala His Pro 75	4
act gat gac acc acg acg Thr Asp Asp Thr Thr Thr 80 85	g ctc tct gag aga cca : Leu Ser Glu Arg Pro 90	tcc cca agc aca kac 39 Ser Pro Ser Thr Xaa 95	2

WO 99/31236 -173 - PCT/IB98/02122

gt	cat	dac	aga	ccp	cba	kda	ccc	tca	akc	cat	ctq	qtt	ttc	atq	agg	440
Va:	His	Xaa	Arg	Pro	Xaa	Xaa	Pro	Ser	Xaa	His	Leu	Val	Phe	Met	Ara	• • • •
				100					105					110	_	
ato	acc	cct	tct	tct	atg	atg	aac	aca	ccc	tcc	gga	aac	sgg	ggc	tat	488
Met	Thr	Pro	ser	Ser	Met	Met	Asn	Thr	Pro	Ser	Gly	Asn	Xaa	Gly	Cys	
			115					120					125			
Egg	tcg	cag	ctg	tgc	tgt	tca	tca	cag	gca	tca	tca	tcc	tca	cca	qtq	536
Trp	Ser	GIN	Leu	Cys	Cys	Ser	Ser	Gln	Ala	Ser	Ser	Ser	Ser	Pro	Val	
		130					135					140				
gca	agt	gca	ggc	agc	tgt	CCC	ggt	tat	gcc	gga	atc	att	gca	ggt	gag	584
Ата	261	Ala	Gly	Ser	Cys	Pro	Gly	Tyr	Ala	Gly	Ile	Ile	Ala	Gly	Glu	
	143					150					155					
000	atc	aga	aac	agg	agc	tgad	caac	ctg (	ctggg	gcaco	cc ga	aaga	ccaa	3		632
Set	TTE	Arg	Asn	Arg	ser											
160				•	165											
CCC	cctg	cca	gctca	ccg	tg c	ccago	cctc	tg:	catco	cct	cgaa	agago	ct q	ggcca	agagag	692
gga	agac	ıca (	gatga	atgaa	ag ct	tggac	ccad	a aad	ctaca	caat	cca	agtci		acct	CCCCC	752
auc	cctg	CC (	gcccc	cgaa	ag go	chaco	ctqq	900	cttac	aga	ctai	ccct	ca a	agtta	atctcc '	812
tct	gcta	aga (	caaaa	agta	aa aq	gcact	gtg	g tct	ttg	caaa	aaaa	aaaaa	a			860
	0 > 2															
	1 > 59	_														
	2> DI															
<21	3 > Ho	omo s	sapie	ns												
20																
<22		_														
	L> CI															
<22	2 > 24	56	50													
<22.	L> 81	g_pe	ptid	e												
	2> 24															
< 22.	5 > VC	n He	ijne	mat	rix											
			10.3													
	se	d ri	rrrc	GPSC	DQC/	RP										
				_												
<223	L> pc	TyA	sign	al												
<222	?> 56	35	68													
<221	.> pc	lyA_	site													
<222	> 58	35	93													
		_														
	> 25															
aano	cago	tg c	sgcc	ggcc	a go	c at	g ga	g ac	t gg	a go	g ct	g cg	g cg	c cc	g caa	53
						Me			r Gl	y Al	a Le	u Ar	g Ar	g Pr	o Gln	
							- 2					- 2				
CCC	CEC	ccg	ttg	ctg	ctg	ctg	ctc	tgc	ggc	cct	tcc	cag	gat	caa	tgc	101
Leu	Leu	Pro	Leu	Leu	Leu	Leu	Leu	Cys	Gly	Pro	Ser	Gln	qzA	Gln	Cys	
	-15					-10					- 5					
cga	cct	gta	ctc	cag	aat	ctg	ttg	cag	agc	cca	ggc	ttg	aca	tgg	agc	149
Arg	Pro	Val	Leu	Gln	Asn	Leu	Leu	Gln	Ser	Pro	Gly	Leu	Thr	Trp	Ser	
1				5					10					15		
ttg	gaa	gtg	CCC	act	<b>999</b>	aga	gaa	gga	aag	gaa	ggt	ggg	gat	cgq	gga	197
Leu	Glu	Val	Pro	Thr	Gly	Arg	Glu	Gly	Lys	Glu	Gly	Gly	Āsp	Arg	Gly	
								25			•	•	30	-		
			20													
cca	999	cta	20 akt	<b>9</b> 99	gcc	act	cca	gcc	agg	agc	cct	caq	ggc	aaq	gag	245
cca Pro	999	cta Leu	20 akt	ggg Gly	gcc Ala	act Thr	cca Pro	gcc Ala	agg Arg	agc Ser	cct Pro	cag Gln	ggc	aag Lys	gag Glu	245
cca Pro	999	cta Leu 35	20	ggg Gly	gcc Ala	Thr	cca Pro 40	gcc Ala	agg Arg	agc Ser	cct Pro	cag Gln 45	ggc	aag Lys	gag Glu	245
ero atg	999 Gly	Leu 35 aga	20 akt Xaa Caa	Gly agg	Ala	Thr aga	Pro 40 aag	Ala	Arg	Ser ggc	Pro	Gln 45 qct	ggc Gly tqq	Lys akt	Glu	
ero atg	999 Gly	Leu 35 aga	20 akt Xaa Caa	Gly agg	Ala	Thr aga	Pro 40 aag	Ala	Arg	Ser ggc	Pro	Gln 45 qct	ggc Gly tqq	Lys akt	Glu	245
ero atg	999 Gly	Leu 35 aga	20 akt Xaa	Gly agg	Ala	Thr aga	Pro 40 aag	Ala	Arg	Ser ggc	Pro	Gln 45 qct	ggc Gly tqq	Lys akt	Glu	

aca gca aat cag gaa cta aac agg atg agg tot otg tot tot ggo too Thr Ala Asn Gln Glu Leu Asn Arg Met Arg Ser Leu Ser Ser Gly Ser	341
65 70 75 80	
gtg cca gtg ggg cat ctg gag ggt ggc acg gtc aag ctt cag aag gac Val Pro Val Gly His Leu Glu Gly Gly Thr Val Lys Leu Gln Lys Asp	389
85 90 95	400
acg gge etc cat tee tge ara gat ggt atg get tet ett gaa ggg acg	437
Thr Gly Leu His Ser Cys Xaa Asp Gly Met Ala Ser Leu Glu Gly Thr	
100 105 110	
cca gct tca gtc ctg gct gat gct tgc cca gga ttc cat gat gtg aan	485
Pro Ala Ser Val Leu Ala Asp Ala Cys Pro Gly Phe His Asp Val Xaa	
115 120 125	
gtt car arg gcc cta ttt ggg tta agt ggg ana rta ctg tgg ctg aaa	533
Val Gln Xaa Ala Leu Phe Gly Leu Ser Gly Xaa Xaa Leu Trp Leu Lys	
130 135 140	
acc cac ttc tgc ctt tct att ana ctt taaataaact ctgaaracct	580
Thr His Phe Cys Leu Ser Ile Xaa Leu	
145 150	
gtaaaaaaa aaa	593
<210> 252	
<211> 1114	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 109558	
7227 103336	
<221> sig peptide	
(221) SIG DEDEIGE	
· · · · · · · · · · · · · · · · · · ·	
<222> 109273	
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	
<222> 109273 <223> Von Heijne matrix score 3.70000004768372	
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	
<222> 109273 <223> Von Heijne matrix score 3.70000004768372 seq VAFMLTLPILVCK/VQ	
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	
<222> 109273 <223> Von Heijne matrix score 3.70000004768372 seq VAFMLTLPILVCK/VQ	
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	60
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	60 117
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117 165 213
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117 165 213
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117 165 213 261
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117 165 213
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117 165 213 261
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	<ul><li>117</li><li>165</li><li>213</li><li>261</li><li>309</li></ul>
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117 165 213 261
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	<ul><li>117</li><li>165</li><li>213</li><li>261</li><li>309</li></ul>
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117 165 213 261 309 357
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	<ul><li>117</li><li>165</li><li>213</li><li>261</li><li>309</li></ul>
<pre>&lt;222&gt; 109273 &lt;223&gt; Von Heijne matrix</pre>	117 165 213 261 309 357

WO 99/31236 -175- PCT/IB98/02122

30 35 40	
ctc ttt ggg atc ctc ttt tcc atc tgc ttc tcc tgc ctg ctg gct cat	453
Leu Phe Gly Ile Leu Phe Ser Ile Cys Phe Ser Cys Leu Leu Ala His	
45 50 . 55 60	
	503
get gte agt etg ace aag ete gte egg ggg agg aaa gee eet tte eet	501
Ala Val Ser Leu Thr Lys Leu Val Arg Gly Arg Lys Ala Pro Phe Pro	
65 70 <b>7</b> 5	
gtt ggt gat tot ggg tot ggc ogt ggg ott dag oot agt oca gga tgt	549
Val Gly Asp Ser Gly Ser Gly Arg Gly Leu Gln Pro Ser Pro Gly Cys	
in the second se	
tat cgc tat tgaatatatt gtootgacca tgaataggac caacgtcaat	598
Tyr Arg Tyr	
95	
gtottttetg agettteege teetegtege aatgaaaact tigteeteet geteacetae	658
kteetettet tgatggeget gaeetteete westeeteet teaeettetg tggtkeette	718
acgggctgga avagacatgg ggcccacate taceteasga tgeteskete cattgecate	778
tgggtggcct ggatcaccct gctcatgctt c <u>ctca</u> ctttg accgcrggtg ggatgacacc	838
atomicarci coycottggs trosaatggo tgggtgttcc tgttggctta tgttagtccc	898
gagttttggc tgctcacaaa gcaackaaac cccatggatt atcctgttga ggatgctttc	958
tgtaaacctc aactcgtgaa gaagagctat ggtgtggrga acagagccta skctcaagag	1018
gaaatcactc aaggttttga agagacaggg gacacgctct atgcccccta ttccacacat	1078
tttcagctgc agaascagcc tccccaaaaa aaaaaa	1114
**	
<210> 253	
<211> 1182	
<212> DNA	
<213> Homo sapiens	
COLOR DEPLOYED	
<220>	
<221> CDS .	
<222> 128835	
222. pie moneido	
<221> sig_peptide	
<222> 128220	
<223> Von Heijne matrix	
score 4.69999980926514	
seg LAVDSWWLDPGHA/AV	
ocq anvaonnableas, av	
<221> polyA_signal	
<222> 11451150 ~ •	
<221> polyA_site	
<222> 11701181	
<400> 253	
aagaactgcg tetegegace caggegeggg tteeeggagg acagecaaca agegatgetg	60
ccgccgccgt ttcctgattg gttgtgggtg gctacctctt cgttctgatt ggccgctagt	120
dadcaad and one and dat one and cod as dad dad dad dad cod codecade frontagenta denderated denderat	169
	-47
Met Leu Ser Lys Gly Leu Lys Arg Lys Arg Glu Glu Glu	
-30 -25 -20	
gag aag gaa cot otg goa gto gao toc*tgg tgg ota gat oot ggo cao	217
Glu Lys Glu Pro Leu Ala Val Asp Ser Trp Trp Leu Asp Pro Gly His	
gea geg geg gea cag gea eee eeg gee geg gee tet age tee ete tet	265
Ala Ala Val Ala Gln Ala Pro Pro Ala Val Ala Ser Ser Ser Leu Phe	
1 5 10 15	
1	313
gae etc tea gtg etc aag etc cac cac age etg cag vrr agt rag eeg	213
Asp Leu Ser Val Leu Lys Leu His His Ser Leu Gln Xaa Ser Xaa Pro	
20 25 30	
20	361
gac ctg cgg cac ctg gtg ctg gtc atr aac act ctg cgg cgc atc cag	361

Asp Leu Arg His Leu Val Leu Val Xaa Asn Thr Leu Arg Arg Ile Gln 35 40 45	
geg tee atg gea eee geg get gee etg eea eet gtg eet ace eea eet	409
Ala Ser Met Ala Pro Ala Ala Ala Leu Pro Pro Val Pro Thr Pro Pro 50 55 60	
gea ged ede ant gtg get gac aac tta etg gea age teg gac get gec	457
Ala Ala Pro Xaa Val Ala Asp Asn Leu Leu Ala Ser Ser Asp Ala Ala 65 70 75	
ctt toa goo too atg goo arm oto otg gar gac etc age cac att gag	505
Leu Ser Ala Ser Met Ala Xaa Leu Leu Glu Asp Leu Ser His Ile Glu 80 85 90 95	
ggc ctg agt cag gct ccc caa ccc ttg gca gac gag ggg cca cca ggc	553
Gly Leu Ser Gln Ala Pro Gln Pro Leu Ala Asp Glu Gly Pro Pro Gly	
100 105 110	601
cgt agc atc ggg gga wca ccg ccc amc ctg ggt gcc ttg gac ctg ctg Arg Ser Ile Gly Gly Xaa Pro Pro Xaa Leu Gly Ala Leu Asp Leu Leu	601
115 120 125	
ggc cca gcc act ggc tgt cta ctg gac aat ggg ctt gag gyc ctg ttt	649
Gly Pro Ala Thr Gly Cys Leu Leu Asp Asn Gly Leu Glu Gly Leu Phe	
130 135 140	
gag gat att gac acc tot atg tat gac aat gaa ott tgg gca cca gcc	697
Glu Asp Ile Asp Thr Ser Met Tyr Asp Asn Glu Leu Trp Ala Pro Ala	
145 150 155 tet gag gge ete aaa eea gge eet gag gat ggg eeg gge aag gag gaa	745
Ser Glu Gly Leu Lys Pro Gly Pro Glu Asp Gly Pro Gly Lys Glu Glu	743
160 165 170 175	
gct ccg gag ctg gac gag gcc gaa ttg gac tac ctc atg gat gtg ctg	793
Ala Pro Glu Leu Asp Glu Ala Glu Leu Asp Tyr Leu Met Asp Val Leu	
180 185 190	225
gtg ggc aca cag gca ctg gag cga ccg ccg ggg cca ggg cgc	835
Val Gly Thr Gln Ala Leu Glu Arg Pro Pro Gly Pro Gly Arg 195 200 205	
tgagccctcg tgctggaatg gttgtctggt atctgaactg agcctgctgg ctggaccaac	895
tgtcctcgaa aagacacage tggcttccct agtacagaga acagggcttg ggccactttg	955
gagagacaga atctagtect gggcaactte acateegtee teetgtetea gggetggcag	1015
ggggagcctg gaattacccc ctagtgatgg aatgacaggg tctggtgggg actgaattcc	1075
ctggccctgg ggtcataget tgggctgttc cttctctgat acgggaagag acccaatcag	1135
atttttcaaa ttaaagccag tootgggaaa totcaaaaaa aaaaaac	1182

```
<210> 254
```

<211> 1073

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 59..505

<221> sig_peptide <222> 59..358

<223> Von Heijne matrix score 3.70000004768372 seq LASSFLFTMGGLG/FI

<221> polyA_signal

<222> 1042..1047

<221> polyA_site

<222> 1062..1073

	)> 29															
act	gttti	ng g	ggag	gcgc	gt gg	gggct	tgaç	gco	gaga	aacg	gcc	ttg	ctg d	caco	aac	58
atg	gag	act	ttg	tac	cgt	gtc	ccg	ttc	tta	gtg	ctc	gaa	tgt	ccc	aac	106
					Arg											
-100	)				- 95					-90			-		-85	
ctg	aag	ctg	aag	aag	ccg	ccc	tgg	ttg	cac	atg	ccg	tcg	gcc	atg	act	154
Leu	Lys	Leu	Lys	Lys	Pro	Pro	Trp	Leu	His	Met	Pro	Ser	Ala	Met	Thr	
				-80					-75					-70		
gtg	tat	gct	ctg	gtg	gtg	gtg	tct	tac	ttc	ctc	atc	acc	gga	gga	ata	202
					Val											
			-65					-60					-55	-		
att	tat	gat	gtt	att	gtt	gaa	cct	cca	agt	gtc	ggt	tct	atg	act	gat	250
Ile	Tyr	Asp	Val	Ile	Val	Glu	Pro	Pro	Ser	Val	Gly	Ser	Met	Thr	Asp	
		-50					-45				•	-40			=	
gaa	cat	ggg	cat	cag	agg	cca	gta	gct	ttc	ttg	gcc	tac	aga	gta	aat	298
					Arg											
	-35					-30					-25	-	_			
gga	caa	tat	att	atg	gaa	gga	ctt	gca	tcc	agc	ttc	cta	ttt	aCa	atg	346
Gly	Gln	Tyr	Ile	Met	Glu	Gly	Leu	Ala	Ser	Ser	Phe	Leu	Phe	Thr	Met	
-20					-15					-10					- 5	
gga	ggt	tta	ggt	ttc	ata	atc	ctg	gac	gga	tcg	aat	gca	cca	aat	atc	394
Gly	Gly	Leu	Gly	Phe	Ile	Ile	Leu	Asp	Gly	Ser	Asn	Ala	Pro	Asn	Ile	
				1				5					10			
cca	aaa	ctc	aat	aga	ttc	ctt	ctt	ctg	ttc	att	gga	ttc	gtc	tgt	gtc	442
Pro	Lys	Leu	Asn	Arg	Phe	Leu	Leu	Leu	Phe	Ile	Gly	Phe	Val	Cys	Val	
		15					20					25				
cta	twr	agt	ttt	tkc	ayg	gct	aga	gta	ttc	atg	aga	atg	aaa	ctg	ccg	490
Leu	Xaa	Ser	Phe	Xaa	Xaa	Ala	Arg	Val	Phe	Met	Arg	Met	Lys	Leu	Pro	
	30				•	35					40					
ggc	tat	ctg	atg	ggt	taga	agtgo	ect t	tgas	saaga	aa a	cagi	tggai	t act	tggat	ttg	545
Gly	Tyr	Leu	Met	Gly												
45																
ctcc	tgto	aa v	vgaas	sttti	ta aa	aggct	gtmo	caa	atcct	ccta	ata	tgaaa	atg 1	tggaa	aaagaa	605
tgaa	gago	ag d	cagta	aaaa	ga aa	atato	ctagi	: gaa	aaaa	acag	gaag	gcgt	att 9	gaag	cttgga	665
ctag	jaatt	tc t	tct	tggta	at ta	aaaga	agaca	a agi	ttat	cac	aga	attt	ttt	ttcci	tgctgg	725
ccta	ttgo	ta t	acca	aatga	at gi	ttgag	gtgg	ati	tttct	ttt	tag	tttt	tca	ttaaa	aatata	785
ttcc	atat	ct a	acaa	ctata	aa ta	atcaa	aataa	a agi	tgati	att	ttt	taca	acc	ctcti	taacat	845
tttt	tgga	iga t	gaca	attt	ct ga	attt	caga	a aa	ttaad	cata	aaa	tcca	gaa	gcaa	gattcc	905
gtaa	gcto	gag a	acto	ctgga	ac ag	gttga	atca	g cti	ttac	ctat	ggt	gctt	tgc ·	cttt	aactag	965
														acaa	taagat	1025
gtat	gaad	gg a	agcag	gaaa	ta a	ataci	ttt	ct	aatta	aaaa	aaa	aaaa	a			1073

```
<210> 255
```

<211> 818

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 1..207

<221> sig_peptide

<222> 1..147

<223> Von Heijne matrix score 7.59999990463257 seq HLPFLLLLSCVGX/XP

<221> polyA_signal <222> 784..789

```
<221> polyA site
<222> 807..818
<400> 255
atg cot tto cat ttt cog tto ott ggg ttt gtg tgt etg cat ctc cat
Met Pro Phe His Phe Pro Phe Leu Gly Phe Val Cys Leu His Leu His
                -45
                                    -40
                                                                      96
ctt acc cct tgc ctg act gta ccc cgt aga ccc ctg ttt ctc ctc ctg
Leu Thr Pro Cys Leu Thr Val Pro Arg Arg Pro Leu Phe Leu Leu Leu
                                - 25
                                                   -20
            -30
cac ctg tgt ecc cat ctg ecc tte ttg ttg etc etg tea tgt gte ggg
His Leu Cys Pro His Leu Pro Phe Leu Leu Leu Ser Cys Val Gly
       - 15
                            -10
                                                                     192
gke www eee tee tgt etg eet tet tee tee aet tgt gte age ttg eat
Xaa Xaa Pro Ser Cys Leu Pro Ser Ser Ser Thr Cys Val Ser Leu His
   1
                                        10
                                                                     247
ttt ttt att oct gac tgagtoacca caccoctoto cootgatoaa agggaatatk
Phe Phe Ile Pro Asp
                20
artttttaat ttggatcgac tgaggtgcca ggagaaactg cagkcccagg tatccmvaca
gecaccagga tggtccctcg ceccacccc accgcctctk ccccaccttt tecaacgtgt
                                                                     367
tgcatgctgg gaactggggg gtgtggggga aggggctgcc ggcttctttc aggangctga
                                                                     427
                                                                     487
rgtttggarg caaaatcaac ctgggaracc accccggccg cggcgcctca gtggacaggt
                                                                     547
gggargaaaa gaaaacttct taccttggar garggacatc ccgcttcctt atccttagct
tttttgttgc tcctccccac tgcccctttt aatttatttg gttgtttgcg gaaggagggg
                                                                     607
                                                                     667
ggaaggggt aagctgggcc gggaactgtc cgaggtgctg agctggggcg ggaccggaat
cctcccggta gggtaccagg gactgagttg ggcctggggc cgtgtccaag gtgccaatga
                                                                     727
                                                                     787
tgcgggccga cagarcgggc cgcactgtct gtctgtccgt ctgtcccgga aagaactata
                                                                     818
aagcgctgga agcgcctgca aaaaaaaaaa a
<210> 256
<211> 971
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 12..734
<221> sig_peptide
<222> 12..101
<223> Von Heijne matrix
      score 4.80000019073486
     seq ILFCVGAVGACTL/SV
<221> polyA signal
<222> 914..919
<221> polyA_site
<222> 961..971
<400> 256
                                                                       50
aatacacaga a atg ggg act gcg agc aga agc aac atc gct cgc cat ctg
             Met Gly Thr Ala Ser Arg Ser Asn Ile Ala Arg His Leu
             -30
                                  -25
                                                                       98
caa acc aat ctc att cta ttt tgt gtc ggt gct gtg ggc gcc tgt act
```

Gln Thr Asn Leu Ile Leu Phe Cys Val Gly Ala Val Gly Ala Cys Thr -10

ctc tct gtc aca caa ccg tgg tac cta gaa gtg gac tac act cat gag Leu Ser Val Thr Gln Pro Trp Tyr Leu Glu Val Asp Tyr Thr His Glu

-15

- 5

146

	1				5					10					15	
gcc	gtc	acc	ata	aag	tgt	acc	ttc	tcc	gca	acc	gga	tgc	CCL	tct	gag	194
Ala	Val	Thr	Ile	Lys	Cys	Thr	Phe	Ser	Ala	Thr	Gly	Cys	Pro	Ser	Glu	•
				20					25					30		
		aca														242
Gln	Pro	Thr	Cys	Leu	Trp	Phe	Arg		Gly	Ala	His	Gln	Pro	Glu	Asn	
			35					40					45			
		ttg														290
Leu	Cys	Leu	Asp	Gly	Cys	Lys		Glu	Ala	Xaa	Lys		Thr	Val	Arg	
		50					55					60				
		ctc														338
GIU	65	Leu	rys	GIU	Asn		vaı	ser	Leu	Thr		Asn	Arg	vai	rnr	
		~~~	201			70					75					206
		gac Asp														386
80	Maii	waħ	261	MIA	85	TAT	116	cys	GIÀ	90	Ald	Pne	210	261	95	
	722	gcg	202	act		C2.0	202	773	~~~		300	202	cta	ata	-	434
		Ala														7.7
110	014	7.4	~- 9	100	575	J 1	****	O1y	105	Gry	1111			110	***	
aga	gaa	att	aaa		ctc	age	ааσ	gaa		caa	age	ttc	cta		act	482
_	-	Ile	_	_		_	_	_	_		_		_		-	
· · · · · J			115				-1-	120		5			125			
ctt	gta	tca		ctc	tct	gtc	tat		acc	ggt	gtg	tgc	gtg	gcc	ttc	530
	_	Ser	_			_						-		_		
		130					135			-		140				
ata	ctc	ctc	tcc	aaa	tca	aaa	tcc	aac	cct	cta	aga	aac	aaa	gaa	ata	578
Ile	Leu	Leu	Ser	Lys	Ser	Lys	Ser	Asn	Pro	Leu	Arg	Asn	Lys	Glu	Ile	
	145					150					155					
		gac														626
Lys	Glu	Asp	Ser	Gln	Lys	Lys	Lys	Ser	Ala	Arg	Arg	Ile	Phe	Gln		
160					165					170					175	
		caa														674
Ile	Ala	Gln	Glu		Tyr	His	Lys	Arg		Val	Glu	Thr	Asn		Gln	
				180					185					190		
		aaa														722
ser	Glu	Lys		Asn	Asn	Thr	Tyr		Asn	Arg	Arg	Val		Ser	ASD	
			195					200					205			774
	_	agg		taga	aaac	gcc :	ccaa	נככנ	ca a	tgaa	gtca	c tg	aaaa	tcca		//4
Tyr	GIU	Arg	Pro													
act		210								a a to a					aa+aaa	834
															aataaa	894
															tataac	954
					La C	Lddd	accc	a aC	adad	cgca	act	yaaa	aaı	actt	tccaaa	971
وعانان	jecai	aaa a	1444	aaw ,												31 L

<210> 257
<211> 640
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 378..518

<221> sig_peptide
<222> 378.467
<223> Von Heijne matrix
score 5.5
seq SLMTCTTLINASA/IS

<221> polyA_signal

```
<222> 607..612
<221> polyA_site
<222> 628..640
<400> 257
agectgggta akgeccaaga tggctgtett egeettaqta etegtgtgaa gttggeggg
                                                                       60
acggttcctg tcatcttctt gggcttattt ggtgtgctgt tgaagggggg agactagaga
                                                                     120
aatggcaggg aacctcttat ccggggcagg taggcgcctg tgggactggg tgcctctggc
                                                                     180
gtgcagaagc ttctctcttg gtgtgcctag attgatcggt ataaggctca ctctcccgcc
                                                                      240
                                                                     300
ccccaaagtg gttgatcgtt ggaacgagaa aagggccatg ttcggagtgt atgacaacat
cgggatcctg ggaaactttg aaaagcaccc caaagaactg atcagggggc ccatatggct
                                                                     360
togaggtigg aaaggga atg aat tgc aac git gta too gaa aga gga aaa
                                                                      410
                   Met Asn Cys Asn Val Val Ser Glu Arg Gly Lys
                   -30
                                       -25
tgg ttg gaa gta gaa tgt tcg ctg atg acc tgc aca acc tta ata aac
                                                                      458
Trp Leu Glu Val Glu Cys Scr Leu Met Thr Cys Thr Thr Leu Ile Asn
                -15
                                    -10
                                                        - 5
                                                                      506
gca tcc gct atc tct aca aac act tta acc gac atg gga agt ttc gat
Ala Ser Ala Ile Ser Thr Asn Thr Leu Thr Asp Met Gly Ser Phe Asp
                                                10
                            5
                                                                      558
aga aga gaa agc tgagaacttc ggaaaaggct catctgtcac cctggaraag
Arg Arg Glu Ser
   15
                                                                      618
ggaaactgta cttttccctg tgaggaaacg gctttgtatt ttctctgtaa taaaatgggg
cttctttgga aaaaaaaaa aa
                                                                      640
<210> 258
<211> 745
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 110..304
<221> sig_peptide
<222> 110..193
<223> Von Heijne matrix
      score 4.59999990463257
      seq PLQWSLLVAVVAG/SV
<221> polyA_signal
<222> 708..713
<221> polyA site
<222> 732..743
<400> 258
acttecgect gegeetgege ageveagete eshgagecet gecaaceatg gtgaacttgg
                                                                       60
gtotgtoccg ggtggacgac gccgtggctg ccaagcaccc ggcaccggc atg gcc ttt
                                                                       118
                                                       Met Ala Phe
ggc ttg cag atg ttc att cag agg aag ttt cca tac cct ttg cag tgg
                                                                       166
Gly Leu Gln Met Phe Ile Gln Arg Lys Phe Pro Tyr Pro Leu Gln Trp
                                                             -10
                    -20
                                         -15
                                                                       214
age etc eta gtg gee gtg gtt gea gge tet gtg gte age tae ggg gtg
Ser Leu Leu Val Ala Val Val Ala Gly Ser Val Val Ser Tyr Gly Val
                -'5
acg aga gtg gag tcg gag aaa tgc aac aac ctc tgg ctc ttc ctg gag
                                                                       262
```

WO 99/31236 -181- PCT/IB98/02122

Thr Arg Val Glu Ser Glu Lys Cys Asn Asn Leu Trp Leu Phe Leu Glu	
10 15 20	204
acc gga cag ctc ccc aaa gac agg agc aca gat cag ara agc	304
Thr Gly Gln Leu Pro Lys Asp Arg Ser Thr Asp Gln Xaa Ser	
25 30 35 taggagaget ceageagggg cacagargat tgggggeagg argartetgg aacacakeet	364
teatgecece tgaceceagg ecgacectee ceacacecta gggtacecea gtegtatect	424
ctgtccgcat gtgtggccag gcctgacaaa cmcctgcaga tggctgctgc cccaacctgg	484
gacctgccca ggaggttgga gcagaaaggg ctctccctgg ggtggtgttt ctcctctagg	544
gtattgggat gcatgttctg cactgccagc agagagggtg tgtctggggg ccaccaccta	604
tgggacacgg ggtcgaaggg gcctgtacac tctgtcattt cctttctagc ccctgcatct	664
ccaacaagtc caaggtgaca gctggtgcta ggggcgtggg gttaataaat ggcttatcct	724
tctctccaaa araaaaaaam c	745
<210> 259	
<211> 637	
<212> DNA	
<213> Homo sapiens	
·	
<220>	
<221> CDS	
<222> 201419	
<221> sig_peptide	
<222> 201272 <223> Von Heijne matrix	
score 6.4000009536743	
seq LSYLPLWLGPIWP/CS	
<221> polyA signal	
<222> 601606	
<221> polyA_site	
<222> 627637	
<400> 259 acaaaatata attgcctcts ccctctccca ttttctctct tgggagcaat ggtcacagtc	60
cotggtacet gaaaaggtac ctaggtetag geeettette cettteeett esteteeet	120
acccagaac tttggctccc tttcccttct ctctctggta gctccaggag gcctgtgatc	180
cageteeetg ectageatee atg ace tgt tgg atg tta eet eea ate agt tte	233
Met Thr Cys Trp Met Leu Pro Pro Ile Ser Phe	
-20 -15	
ctg tcc tac ctg cct ctt tgg ctt gga cct ata tgg cca tgc tct ggc	281
Leu Ser Tyr Leu Pro Leu Trp Leu Gly Pro Ile Trp Pro Cys Ser Gly	
-10 -5	329
tot acc off ggg aag oof gat ood ggt gtg tgg cod ago ftg tto agg	349
Ser Thr Leu Gly Lys Pro Asp Pro Gly Val Trp Pro Ser Leu Phe Arg	
5 10 15	377
ccc tgg gat gct gca tct cca ggc aac tat gca ctt tcc cgg gga rar	• • •
Pro Trp Asp Ala Ala Ser Pro Gly Asn Tyr Ala Leu Ser Arg Gly Xaa	
20 25 30 aac cak tat gav aak tgg ggg cag ggc aca cat tca tct ttg	419
Asn Xaa Tyr Xaa Xaa Trp Gly Gln Gly Thr His Ser Ser Leu	
40 45	
targaaggte tggcctgggg terggtgaag gagggeccag gteagttetg gggteccagt	479
qacctqcttt qccattctcc tggtgccgct gctgctccct gtttctggag ctggatgttc	539
cccacctggc agttgagctg cctgagccaa tgtgtctgtc tttggtaact gagtgaacca	599
taataaaggg gaacatttgg ccctgtgaaa aaaaaaaa	637

```
<210> 260
<211> 1315
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 123..302
<221> sig peptide
<222> 123..176
<223> Von Heijne matrix
     score 4.30000019073486
      seq WTCLKSFPSPTSS/HA
<221> polyA_signal
<222> 1279..1284
<221> polyA_site
<222> 1301..1312
<400> 260
aagagcatcc tgcgccccgg cgcggggccc tgcggtagcc tcaggcccct cccctggacc
cgccgcagag ccagtgcaga atacagaaac tgcagccatg accacgcacg tcaccctgga
                                                                   120
ag atg ccc tgt cca acg tgg acc tgc ttg aag agc ttc ccc tcc ccg
                                                                   167
   Met Pro Cys Pro Thr Trp Thr Cys Leu Lys Ser Phe Pro Ser Pro
               -15
                                   -10
acc age age cat gea teg age etc cae ett eet eea tea tgt acc agg
                                                                   215
Thr Ser Ser His Ala Ser Ser Leu His Leu Pro Pro Ser Cys Thr Arg
                            5
cta act ttg aca caa act ttg agg aca gga atg cat ttg tca cgg gca
                                                                    263
Leu Thr Leu Thr Gln Thr Leu Arg Thr Gly Met His Leu Ser Arg Ala
                        20
                                           25
                                                                    312
ttg caa ggt aca ttg acc agg cta cag tcc act cca gca tgaatgarat
Leu Gln Gly Thr Leu Thr Arg Leu Gln Ser Thr Pro Ala
                                       40
                    35
gctggaggaa ggacatgakt atgcggtcat gctgtacacc tggcgcagct gttcccgggc
                                                                    372
                                                                    432
cattecceag gtgaaatgca acrageagee caacegakta raratetatg araaracagt
                                                                    492
araggtgctg gagccggagg tcaccaagct catgaagttc atgtattttc arcgcaaggc
                                                                    552
catcgagcgg ttctgcascg aggtgaagcg gctgtgccat gccgagcgca ggaaggactt
tgtctctgag gcctacctcc tgacccttgg caagttcatc aacatgtttg ctgtcctgga
                                                                    612
tgagctaaag aacatgaast gcagcgtcaa raatgaccac tctgcctaca agagggcagc
                                                                    672
acagttcctg cggaagatgg cagatcccca gtctatccag gagtcgcaga acctttccat
                                                                    732
gttcctggcc aaccacaaca ggatcaccca gtgtctccac cagcaacttg aagtgatccc
                                                                    792
                                                                    852
aggctatgag gagctgctgg ctgacattgt caacatctgt gtggattact acgagaacaa
                                                                    912
gatgtacctg actcccagtg agaaacatat gctcctcaag gtaaaactcc cctgaggccg
cacccatgga gcctgggctt accctctcac cttcttctta ttaaaaatcc gttttaaaaa
                                                                   972
acaatgtttc ttttttctta aacattgata cagatcttac ggcacataat ggtttgtaac
                                                                   1032
ctgttccttt cctgtaatat aatataccgt agtcaccttt ccagatgtca ttaaggctat
                                                                   1092
ttctacaatg ttatgtgtaa tgactgccaa gtattctgtt gtattggaac attgtcatgt 1152
aacatatccc ctgtggttgg atatttgcta aacttcattg aacacccttg tagcagtttt 1212
tgtgcacatc tttttgtcaa ggcaaacttc ctagaagaga aattgctggc tcaaagggaa 1272
```

<210> 261 <211> 1035

<212> DNA

<213> Homma sapiens

WO 99/31236 -183 - PCT/IB98/02122

<220>

<221> CDS <222> 98673	
<221> sig_peptide <222> 98.376 <223> Von Heijne matrix score 5.59999990463257 seq VLLLRQLFAQAEK/WY	
<221> polyA_site <222> 10251035	
<400> 261 aattttcygt ggtccaacta ccctcggcga temcaggctt ggcggggcac cgcctggcct ctcccgttcc tttaggctgc cgccgctgcc tgccgcc atg gca gag ttg ggc cta Met Ala Glu Leu Gly Leu -90	60 115
aat gag cac cat caa aat gaa gtt att aat tat atg cgt ttt gct cgt Asn Glu His His Gln Asn Glu Val Ile Asn Tyr Met Arg Phe Ala Arg -85 -80 -75	163
tca aag aga ggc ttg aga ctc aaa act gta gat tcc tgc ttc caa gac Ser Lys Arg Gly Leu Arg Leu Lys Thr Val Asp Ser Cys Phe Gln Asp	211
ctc aag gag agc agg ctg gtg gag gac acc ttc acc ata gat gaa gtc Leu Lys Glu Ser Arg Leu Val Glu Asp Thr Phe Thr Ile Asp Glu Val	259
tot gaa gto oto aat gga tta caa got gtg gtt cat agt gag gtg gaa Ser Glu Val Leu Asn Gly Leu Gln Ala Val Val His Ser Glu Val Glu	307
tot gag oto ato aac act goo tat acc aat gtg tta ott otg oga cag Ser Glu Leu Ile Asn Thr Ala Tyr Thr Asn Val Leu Leu Leu Arg Gln	355
-20 -15 -10 ctg ttt gca caa gct gag aag tgg tat ctt aag cta cag aca gac atc Leu Phe Ala Gln Ala Glu Lys Trp Tyr Leu Lys Leu Gln Thr Asp Ile	403
-5 1 5 tot gaa ott gaa aac oga gaa tta tta gaa caa ktt goa gaa ttt gaa Ser Glu Leu Glu Asn Arg Glu Leu Leu Glu Gln Xaa Ala Glu Phe Glu	451
aaa gca rav att aca tct tca aac aaa aag ccc atc tta dat gtc aca Lys Ala Xaa Ile Thr Ser Ser Asn Lys Lys Pro Ile Leu Xaa Val Thr	499
aas cca aaa ctt gct cca ctt aat gaa ggt gga aca gca aaa ctc cta Xaa Pro Lys Leu Ala Pro Leu Asn Glu Gly Gly Thr Ala Lys Leu Leu	547
45 50 55 aac aag gta ata tgt att ttg aga aac gga aag tct ctc att ctg Asn Lys Val Ile Cys Ile Ile Leu Arg Asn Gly Lys Ser Leu Ile Leu	595
60 65 70 tcc tgt cat tgc cta ggg tgg aga aac aaa agt gga agg ttt gtt tca Ser Cys His Cys Leu Gly Trp Arg Asn Lys Ser Gly Arg Phe Val Ser	643
75 80 85 ggt cct ctg agg ata att agt cca ttg cag tagttttact tgatggtacc Gly Pro Leu Arg Ile Ile Ser Pro Leu Gln	693
90 95 ccatgggcca gaagagggca tacttaacct tctagagagc ctgaagtagc tcctgatcac accttttcaa ggtaaagtga agagcatgaa atttttggaca gcgtttattg atggacattt aaagtttgtg atctgcggta acaaggagaa gggtttttaa gtttaacaaa attatttatc	753 813 873 933
aattagccgg gtgtggtgt acgtgcctat agtcagagct actcgggagg ctgaggcagg agaattgctt gaacccggga ggtggaggtt gcagtgagct gagatcacgc cactgcactc tagcctgggc gacagagcga gactccatct caaaaaaaaa aa	993

```
<210> 262
<211> 696
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 17..463
<221> sig_peptide
<222> 17..232
<223> Von Heijne matrix
     score 3.79999995231628
     seq LMGLALAVYKCQS/MG
<221> polyA_signal
<222> 657..662
<221> polyA site
<222> 684..696
<400> 262
actcaaacag attccc atg aat ctc ttc atc atg tac atg gca ggc aat act
                                                                      52
                  Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr
                          -70
atc tcc atc ttc cct act atg atg gtg tgt atg atg gcc tgg cga ccc
                                                                     100
Ile Ser Ile Phe Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro
                                        -50
                    - 55
                                                                      148
att cag gca ctt atg gcc att tca gcc act ttc aag atg tta gaa agt
Ile Gln Ala Leu Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser
                                    -35
                -40
                                                                      196
tca age cag aag ttt ctt cag ggt ttg gte tat ete att ggg aac etg
Ser Ser Gln Lys Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu
           -25
                                -20
                                                    -15
atg ggt ttg gca ttg gct gtt tac aag tgc cag tcc atg gga ctg tta
Met Gly Leu Ala Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu
                            -5
        -10
cct aca cat gca tcg gat tgg tta gcc ttc att gag ccc cct gag aga
                                                                      292
Pro Thr His Ala Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg
                                         15
                    10
atg gag toa gtg gtg gag gac tgc ttt tqt gaa cat gag aaa gca gcg
Met Glu Ser Val Val Glu Asp Cys Phe Cys Glu His Glu Lys Ala Ala
                                     30
                25
cet ggt eec tat gta tit ggg tet tat tia eat eet tet tia age eea
                                                                      388
Pro Gly Pro Tyr Val Phe Gly Ser Tyr Leu His Pro Ser Leu Ser Pro
                                 45
            40
gtg gct cct cag cat act ctt aaa cta atc act tat gtt aaa aaa aac
Val Ala Pro Gln His Thr Leu Lys Leu Ile Thr Tyr Val Lys Lys Asn
                             60
                                                                      483
caa aaa act ctt ttc tcc atg gtg ggg tgacaggtcc taaaaggaca
Gln Lys Thr Leu Phe Ser Met Val Gly
                         75
    70
atgtgcatat tacgacaaac acaaaaaaac tataccataa cccagggctg aaaataatgt
                                                                      543
                                                                       603
aaaaaacttt atttttgttt ccagtacaga gcaaaacaac aacaaaaaaa cataactatg
                                                                       663
taaacaaaaa aataactgct gctaaatcaa aaactgttgc agcatctcct ttcaataaat
                                                                       696
taaatggttg araacaatgc aaaaaaaaaa aaa
```

<210> 263 <211> 868

```
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 263..481
<221> sig_peptide
<222> 263..322
<223> Von Heijne matrix
      score 11.1999998092651
      seq ILVVLMGLPLAQA/LD
<221> polyA_site
<222> 858..868
<400> 263
                                                                      60
aagacacgcc tacgattaga ctcaggcagg cacctaccgg cgagcggccg cl/gtgactc
ccaggogogg oggtacotca oggtggtgaa ggtcacaggg ttgcagcact cccagtagac
                                                                     120
caggagetee gggaggeagg geeggeeeea egteetetge geaceaceet gagttggate
ctctgtgcgc cacccctgag ttggatccag ggctagctgc tgttgacctc cccactccca
cgctgccctc ctgcctgcag cc atg acg ccc ctg ctc acc ctg atc ctg gtg
                         Met Thr Pro Leu Leu Thr Leu Ile Leu Val
                                                                     340
gto oto atg ggo tta cot otg goo cag goo ttg gao tgo cac gtg tgt
Val Leu Met Gly Leu Pro Leu Ala Gln Ala Leu Asp Cys His Val Cys
-10
                   -5
                                        1
ged tad aad gga gad aad tgd ttd aad ddd atg cgd tgd deg gdt atg
                                                                     388
Ala Tyr Asn Gly Asp Asn Cys Phe Asn Pro Met Arg Cys Pro Ala Met
                                                    20
           10
                                15
gtt gcc tac tgc atg acc acg cgc acc tac tac acc ccc acc agg atg
                                                                     436
Val Ala Tyr Cys Met Thr Thr Arg Thr Tyr Tyr Thr Pro Thr Arg Met
                                               35
        25
                            30
                                                                     481
aag gtc agt aag tcc tgc gtg ccc cgc tgc ttc gar nac tgt gta
Lys Val Ser Lys Ser Cys Val Pro Arg Cys Phe Glu Xaa Cys Val
                        45
                                                                      541
tgatggctac tccaagcacg cgtccaccac ctcctgctgc cagtacgacc tctgcaacgg
caccggcctt gccaccccgg ccaccctggc cctggccccc atcctcctgg ccaccctctg
gggtctcctc taaagccccc gaggcagacc cactcaagaa caaagctctc gagacacact
                                                                      661
getayaccet ekcacceake teaccetgee teacceteca caetecetge gaceteetea
                                                                      721
                                                                      781
gccatgccca gggtcaggac tgtgggcaag aagacacccg acctccccca accaccacac
                                                                      841
gacctcactt cgaggccttg acctttcgat gctgtgtggg atcccaaaag tgtccggctt
tgatgggctg atcagcaaaa aaaaaaa
```

<210> 264

<211> 775

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 42..299

<221> sig_peptide

<222> 42..101

<223> Von Heijne matrix score 5.40000009536743 seq WFVHSSALGLVLA/PP

<221> polyA_site

<222> 762..775 <400> 264 56 aacgatacaa atggtaggcc ttcatgtgag ccagtdacta c atg aat ctt cat ttc Met Asn Leu His Phe -20 104 cca cag tgg ttt gtt cat tca tca gcg tta ggc ttg gtc ctg gct cca Pro Gln Trp Phe Val His Ser Ser Ala Leu Gly Leu Val Leu Ala Pro -10 -5 cct ttc tcc tct ccg ggc act gac ccc acc ttt ccg tgt att tac tgt 152 Pro Phe Ser Ser Pro Gly Thr Asp Pro Thr Phe Pro Cys Ile Tyr Cys 10 agg cta tta aat atg atc atg acc cgc ctt gca ttt tca ttc atc acc 200 Arq Leu Leu Asn Met Ile Met Thr Arg Leu Ala Phe Ser Phe Ile Thr 25 tgt tta tgc cca aat tta aag gaa gtt tgt ctc att ttg cca gaa aaa Cys Leu Cys Pro Asn Leu Lys Glu Val Cys Leu Ile Leu Pro Glu Lys 40 296 aat tgt aat agt cga cac gct gga ttt gta ggg cca sca aaa ttg cgg Asn Cys Asn Ser Arg His Ala Gly Phe Val Gly Pro Xaa Lys Leu Arg 60 55 349 cag tgaaactwkk ttcwcttcta aagcccttca tttcccacaa ggttaagctc Gln togaaacccc atttgatcct tggttcctat ttcgatcctc ctttggaatc tgaaaatcgg 409 469 totocatgtt gratgoaaat taaaakttgo ottgtttgtt actottocaa cacagggtat cagggaraaa gaggcottat otgttootoo atococotg ttttgacaga otgotaagaa 529 ttcctcagga cttcctttgg ttggggattt tactttccca aaagtctgat ctgatttctt 589 649 tcaggggtag acaagcttgt cctagtgctc tgcttcaggt cttatcagaa gaaacccagg aatagaaaag gtagatgcct tgacttttgt ccctgttgtg gggactaaag tgttttttgc 709 769 775 aaaaaa <210> 265 <211> 1075 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 198..431 <221> sig_peptide <222> 198..260 <223> Von Heijne matrix score 6.90000009536743 seq LLACGSLLPGLWQ/HL <221> polyA_site <222> 1064..1074 <400> 265 60 atatatttct gaggcagtac ccatctcact tgtaaactta aaagacaccg cagagatttg agggactcag aagtcaaata gagtaggtta aaaacctctt atttttcaaa ttaattgttt 120 taagaaacaa gcatacctgt gtaagtgaaa tatcttaatt tgtgttgaat caagttagga 180 230 gacagagatt ctcatga atg tgt cct gtg ttc tca aag cag ctg cta gcc

Met Cys Pro Val Phe Ser Lys Gln Leu Leu Ala

-15

278

-20

-10

tgt ggg tct ctc cta cct ggg tta tgg cag cac ctc aca gcc aat cac

Cys Gly Ser Leu Leu Pro Gly Leu Trp Gln His Leu Thr Ala Asn His

WO 99/31236 -187 - PCT/IB98/02122

tgg cet eca tte tee set tte ete tgt aca gtt tge tet ggt tee tea	326
Trp Pro Pro Phe Ser Xaa Phe Leu Cys Thr Val Cys Ser Gly Ser Ser	254
gag cag att tcc gag tat act gct tca gcc acg ccc cca ctg tgc cgt Glu Gln Ile Ser Glu Tyr Thr Ala Ser Ala Thr Pro Pro Leu Cys Arg	374
25 30 35 tcc ctg aac caa gag cca ttc gty tca aga gcc att cgt cca aag tac Ser Leu Asn Gln Glu Pro Phe Val Ser Arg Ala Ile Arg Pro Lys Tyr	422
40 45 50	471
tot atc acc tagecattgt akccatacca ageogggett cetaetteec . Ser Ile Thr 55	471
totgotocco tiggittoct cotginaari aaatotoaci gaccotigai goasciocaa	531
gcatatataa tatatata ataaaaccat abtctaaaaa attcaaacca ggawaaataa	591
asccaraaat ttgtatggga aaaatctgca caaatttatt tggccagcat ggttatcatg	651
gctctattga atttatcctt gaccgtcttt aaagccaaag caaacgggat aaagtgatca	711
actacttacc teteaatacc aaaaargaag caggaggcaa aateteteaw taattteata	771
aaaacaatto ttaketggge geggtggete weacetgtar teccaacact ttgggaggee	831 891
saggtgggcg gatcatgagg tcgggagatc aamaccatcc tggctaacat ggtgaaaccc	951
catototact aaaattacaa aaaattrgot gggcgaggtg gcgggcacct gtggtcccag ctactcggga ggctgaggca agagaatggt gtgaacccca gggggcggag cctgcagtga	1011
getgagateg caccactgea etecageetg ggegacagtg agaeteegte teaaaaaaaa	1071
aaah	1075
<210> 266	
<211> 981	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS <222> 279473	
2225 275473	
<221> sig_peptide	
<222> 279362	
<223> Von Heijne matrix	
score 4.40000009536743	
seq SCFLVALIIWCYL/RE	
<221> polyA_signal	
<222> 944949	
222 2102 240	
<221> polyA_site <222> 970981	
(222) 5/0561	
<400> 266	
agaatcgtgt cttgtgtgcc ccggcggccg ggtgagctcc tcaaggtctc ggagggccga	60
qqqcaqacac cqqcqqqcqq gcgqasqctt actgctctct ctcttccagg gccgtccggg	120
cgctgaggct cataggctgg gcttcccgaa gccttcatcc gttgcccggt tcccgggatc	180
qqqcccaccc tqccqccqaq gaagaggacg accctgaccg ccccattgag ttttcctcca	240
gcaaagccaa coctcacege togtoggtog gccatace atg gga aag gga cat cag	296
Met Gly Lys Gly His Gin	
-25	244
egg ecc tgg tgg aag gtg etg ecc etc age tge tte etc gtg geg etg	344
Arg Pro Trp Trp Lys Val Leu Pro Leu Ser Cys Phe Leu Val Ala Leu	
-20 -15 -10	392
atc atc tgg tgc tac ctg agg gag gag agc gag gcg gac cag tgg ttg	374
Ile Ile Trp Cys Tyr Leu Arg Glu Glu Ser Glu Ala Asp Gln Trp Leu 10	
-5	440
aga cag gtg tgg gga gag gtg cca gag ccc agt gat cgt tct gag gag	•••

Arg Gln Val Trp Gly Glu Val Pro Glu Pro Ser Asp Arg Ser Glu Glu 15 20 25	
cet gag act cca gct gcc tac aga gcg aga act tgacggggtg cccgctgggg Pro Glu Thr Pro Ala Ala Tyr Arg Ala Arg Thr 30	493
ctggcaggaa gggagccgac asccgcctt cggatttgat ktcacgtttg cccgtgactg tcctggctat gcktgcgtcc tcagcactra argacttggc tggtggatgg ggcacttggc tatgctgatt cgcgtgaagg cggavcaaaa tctcagcaaa tcggaaactg ctcctcscct ggctcttgat ktccaaggat tccatcggca aaacttctca ratccttggg gaaggtttca gttgcactgt atgctgttg atttgccaag tctttgtata acataatcat gtttccaaag cacttctggt gacacttgtc atccagtgtt agtttgcagg taatttgctt tctgagatag aatatctggc agaagtgtga aactgtattg catgctgcgg cctgtgcaag gaacacttcc acatgtgagt tttacacaac aacaaatgaa aataaatttt aattttataa tatgggaaaa aaaaaaaa	553 613 673 733 793 853 913 973 981
<210> 267	
<211> 1031	
<212> DNA <213> Homo sapiens	
<220>	
<221> CDS	
<222> 12644	
<221> sig_peptide	
<222> 1292 <223> Von Heijne matrix	
score 4	
seq LTFFSGVYGTCIG/AT	
<221> polyA_signal <222> 10021007	
<221> polyA_site	
<222> 10201031	
<400> 267	50
acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg Met Leu Leu Ser Ile Thr Thr Ala Tyr Thr Gly Leu -25 -20 -15	30
qaa tta act ttc ttc tct ggt gta tat gga acc tgt att ggt gct aca	98
Glu Leu Thr Phe Phe Ser Gly Val Tyr Gly Thr Cys Ile Gly Ala Thr -10 -5 1	
aat aaa ttt gga gca gaa gag ara agc ctt att gga ctt tct ggc att	146
Asn Lys Phe Gly Ala Glu Glu Xaa Ser Leu Ile Gly Leu Ser Gly Ile	
5 10 15 ttc atc ggc att gga gaa att tta ggt gga agc ctc ttc ggc ctg ctg	194
Phe Ile Gly Ile Gly Glu Ile Leu Gly Gly Ser Leu Phe Gly Leu Leu	
20 25 30 agc aag aac get tet ggt aga aat coa get geg etg teg ggc acc	242
Ser Ivs Asn Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly Ile	
Ser Lys Asn Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly Ile 35 40 45 50	
Ser Lys Asn Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly Ile 35 40 45 50 ctq qtq cac ttc ata qct ttt tat cta ata ttt ctc aac atg cct gga	290
Ser Lys Asn Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly Ile 35 40 45 50 ctg gtg cac ttc ata gct ttt tat cta ata ttt ctc aac atg cct gga Leu Val His Phe Ile Ala Phe Tyr Leu Ile Phe Leu Asn Met Pro Gly	290
Ser Lys Asn Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly Ile 35 40 45 50 ctg gtg cac ttc ata gct ttt tat cta ata ttt ctc aac atg cct gga Leu Val His Phe Ile Ala Phe Tyr Leu Ile Phe Leu Asn Met Pro Gly 55 60 65 gat gcc ccg att gct cct gtt aaa gga act gac agc agt gct tac atc	290
Ser Lys Asn Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly Ile 35 40 45 50 ctg gtg cac ttc ata gct ttt tat cta ata ttt ctc aac atg cct gga Leu Val His Phe Ile Ala Phe Tyr Leu Ile Phe Leu Asn Met Pro Gly 55 60 65 gat gcc ccg att gct cct gtt aaa gga act gac agc agt gct tac atc Asp Ala Pro Ile Ala Pro Val Lys Gly Thr Asp Ser Ser Ala Tyr Ile	
Ser Lys Asn Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly Ile 35 40 45 50 ctg gtg cac ttc ata gct ttt tat cta ata ttt ctc aac atg cct gga Leu Val His Phe Ile Ala Phe Tyr Leu Ile Phe Leu Asn Met Pro Gly 55 60 65 gat gcc ccg att gct cct gtt aaa gga act gac agc agt gct tac atc	

95 gga aac agc tgc ttt aat acc cas ctg ctt akt atc tkg	
	igo ttt ota 434
Gly Asn Ser Cys Phe Asn Thr Xaa Leu Leu Xaa Ile Xaa	Sly Phe Leu
100 105 110	
tat tot gaa rac ago goo coa koa ttt goo ato tto aat	tt gtt cag 482
Tyr Ser Glu Xaa Ser Ala Pro Xaa Phe Ala Ile Phe Asn	Phe Val Gln
115 120 125	130
tet att tge gea gee gtg gea ttt tte tae age aac tae	ett ctc ctt 530
Ser Ile Cys Ala Ala Val Ala Phe Phe Tyr Ser Asn Tyr	Leu Leu
135 140	145
cac tgg caa ctc ctg gtc atg gtk atw ttt ggg ttt ttk	ga aca att 578
His Trp Gln Leu Leu Val Met Val Ile Phe Gly Phe Xaa	Hy Thr Ile
150 155	160
ect the the act gig gaa tgg gaa set gee gee thi gia	
Ser Phe Phe Thr Val Glu Trp Glu Xaa Ala Ala Phe Val	(aa Arg Gly
165 170 175	
tot gad tackega agt ato tgatotggtg teegtgaggg gadacg	atg 674
Ser Asp Tyr Arg Ser Ile 180	
acctcagaaa cacagetgga cacagagett ggtggaagaa gtegeett	g atcttcacta 734
tatattgggt gatgttcagt atggaaaatc aagggattaa gactgtta	=
kggtgttca agtttacaga tatgagttat ttaaagcaag tagaataa	
etgtcaactg taattgttca aagatgttgt ttttcatttc atctatct	
catgitata gaatgiaaat gittictici ciciccigci citgiigg	aa gatcctgcct 974
gatttagaa tactaggcca tatgtcatat aaatattttt totggaaa	
-	
<220>	
<221> CDS	
<221> CDS	
<221> CDS <222> 91459 <221> sig_peptide	
<221> CDS <222> 91459 <221> sig_peptide <222> 91330	
<221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix	
<221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix score 7.69999980926514	
<221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix	
<221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix score 7.69999980926514 seq LVLFLSLALLVTP/TS	
<221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix	
<221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix	
<221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix	
<221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix	at tttcaaatac 60
<221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix	
<pre><221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix</pre>	ttg gca ctt 114
<pre> <221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix</pre>	ttg gca ctt 114
<pre><221> CDS <222> 91459 </pre> <pre><221> sig_peptide <222> 91330 </pre> <pre><223> Von Heijne matrix</pre>	ttg gca ctt 114 Leu Ala Leu -75
221> CDS 222> 91459 222> 91459 222> 91330 223> Von Heijne matrix	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162
221> CDS 222> 91459 222> 91459 222> 91330 223> Von Heijne matrix	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162
<pre> <221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix</pre>	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162 Leu Ser Leu
221> CDS 222> 91459 222> 91330 223> Von Heijne matrix	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162 Leu Ser Leu cag act aat 210
221> CDS 222> 91459 222> 91330 223> Von Heijne matrix	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162 Leu Ser Leu cag act aat 210
<pre><221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix</pre>	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162 Leu Ser Leu cag act aat 216 Gln Thr Asn
<pre>c221> CDS c222> 91459 c221> sig_peptide c222> 91330 c223> Von Heijne matrix</pre>	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162 Leu Ser Leu cag act aat 216 Gln Thr Asn tgg gca ttt 25
<pre><221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix</pre>	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162 Leu Ser Leu cag act aat 216 Gln Thr Asn tgg gca ttt 25
<pre><221> CDS <222> 91459 <221> sig_peptide <222> 91330 <223> Von Heijne matrix</pre>	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162 Leu Ser Leu cag act aat 216 Gln Thr Asn tgg gca ttt 25 Trp Ala Phe -25
seq LVLFLSLALLVTP/TS <221> polyA_site <222> 12711281 <400> 268 tattccttgg agttccacga ctgaattaag actgttgtgg grdccatattgcctata ttcgtgttga gggttcacac atg agc aca tgg tat Met Ser Thr Trp Ty: -80 aat aag too tat aag aat aaa gac agc gtt agg att tat Asn Lys Ser Tyr Lys Asn Lys Asp Ser Val Arg Ile Tyr -70 -65 -60 tgc aca gtg agc att aaa ttt aca tac ttt cat gat ata Cys Thr Val Ser Ile Lys Phe Thr Tyr Phe His Asp Ile -55 -50 -45 tgt ctt aca aca tgg aaa cat tcg aga tgc aga ttt tat Cys Leu Thr Thr Trp Lys His Ser Arg Cys Arg Phe Tyr	ttg gca ctt 114 Leu Ala Leu -75 ctc agc ttg 162 Leu Ser Leu cag act aat 216 Gln Thr Asn tgg gca ttt 25 Trp Ala Phe -25 ttg ttc cta 30

-20 -15 -10	254
agc ctg gcc ctg tta gtg aca ccc act tcc acc cct tct gct aar ata Ser Leu Ala Leu Leu Val Thr Pro Thr Ser Thr Pro Ser Ala Lys Ile	354.
-5 1 Set that Fig. 5	
car age ett caa att gac ete eet gga gge tgg agg etg gee aet gac	402
Gln Ser Leu Gln Ile Asp Leu Pro Gly Gly Trp Arg Leu Ala Thr Asp	
10 15 20	
agg atc ttt acc ctc tcc ccc gta ccc atg gac rgc ccc ctc atc ctt	450
Arg Ile Phe Thr Leu Ser Pro Val Pro Met Asp Xaa Pro Leu Ile Leu	
25 30 35 40	
cat cag ttg taaaggtaga tatttgttcc ttggagtcca acatcatgct	499
His Gln Leu	
gttcagaata taatgagatc aatagttgaa aaactagata tacatgccac ccwgacaaag	559
ctattaagtt attaagtgtc agccctggat cttggcttat tgtgaaatgt taattatttt	619
atcactcyat taagaagctg tgggctccat ctcagcattg aaaagggact aatttgctct	679
gttttggaat tgaattaget tteaggeeas cagggeactg tttggtaaat tgetttttee	739 799
agtactagea tgttttctcc ctccatagec tetgttaget tetgagettg taacetecag	859
ggaaavatga gaatatteac cettttaata tgtgtagaga ceatgeaaga ceattgtett ctaataatta gaaataetta gecagattet etatagtaaa ceeggagatt gggagggetg	919
ctttctactt ggtgcatcct tctgcgcttc taatgatttt taaaaatctg ttaataattg	979
atqttttctq qctqqqcaca qtggctcacg cctgtaatcc cagcactttg ggaggccaag	1039
gagggcagat catgaggtca ggagattgar accatectgg ctaacacggt gaaaccccgt	1099
ctctactaaa aatacaaaar aattakccgg gcatggtagt gggcgcctgt gtacccagct	1159
actggggagg ctgaggcarg araatcgctt gaacctggga ggcggaggtt gcastragct	1219
gagatggtgc caccgcactc tagcctgggt gacagagcga gacttcattt caaaaaaaaa	1279
aamc	1283
<210> 269	
<211> 1777	
<212> DNA	
<213> Homo sapiens	
•••	
<220> <221> CDS	
<222> CDS <222> 70327	
(222) (032)	
<221> sig_peptide	
<222> 70147	
<223> Von Heijne matrix	
score 9.60000038146973	
seq WLIALASWSWALC/RI	
<221> polyA_signal	
<222> 17411746	
non control of the	
<221> polyA_site	
<222> 17631774	
<400> 269	
ageceggttt egtgecegeg geegaetgeg casetgteeg egagtetgag ataettacag	60
agagetaca atg gaa aag tee tgg atg etg tgg aac ttt gtt gaa aga tgg	111
Met Glu Lys Ser Trp Met Leu Trp Asn Phe Val Glu Arg Trp	
-25 -20 -15	
cta ata gcc ttg gct tca tgg tct tgg gct ctc tgc cgt att tct ctt	159
Leu Ile Ala Leu Ala Ser Trp Ser Trp Ala Leu Cys Arg Ile Ser Leu	
-10 -5 1	
tta cct tta ata gtg act ttt cat ctg tat gga ggc att atc tta ctt	207
Leu Pro Leu Ile Val Thr Phe His Leu Tyr Gly Gly Ile Ile Leu Leu	
5 10 15 20	
ting tha ata the ata the atw kea ggt att ong tat aaa the cas gat	255

30

303

50

98

Leu Leu Ile Phe Ile Ser Ile Xaa Gly Ile Leu Tyr Lys Phe Xaa Asp

gta ttg ctt tat ttt ccw kaa cag yya tcc tct tca cgt ctt tat gat

Val Leu Leu Tyr Phe Pro Xaa Gln Xaa Ser Ser Ser Arg Leu Tyr Asp

25

<400> 270

```
45
            40
tcc cat gcc cac tgg cmt tcg rca taaaaaaatt ttcatcagaa ccaaagatgg
                                                                     357
Ser His Ala His Trp Xaa Ser Xaa
                                                                     417
aatacgtctg aatcttattt tgatacgata cactggagac aattcaccct attccccaac
                                                                     477
tataatttat tttcatggga atgcaggcaa cataggtcac aggttggcca aatgcattac
ttatgttggt taacctcaaa gttaaccttt tgctggttga ttatcgagga tatggaaaaa
                                                                     537
gtgaaggaga agcaagtgaa gaaggactot acttagatto tgaagctgtg ttagactacg
                                                                     597
tgatgactag acctgacctt gataaaacaa aaatttttct ttttggccgt tccttgggtg
                                                                     657
garcagtggc tattcatttg gcttctgaaa attcacatag gatttcagcc attatggtgg
                                                                     717
                                                                     777
agaacacatt tttaagcata ccacatatgg ceagcacttt attttcattc tttccgatgc
gttaccttcc tttatggtgc tacaaaaata aatttttgtc ctacagaaaa atctctcagt
                                                                     837
gtagaatgcc ttcacttttc atctctggac tctmgatca attaattcca ccagtaatga
                                                                     897
tgaaacaact ttatgaactc tccccatctc ggactaagan attagccatt tttccagatg
                                                                     957
ggactcacaa tgacacatgg cagtgccaag gctatttcac tgcacttgaa cagttcatca
                                                                    1017
                                                                    1077
aaqaaqtcqt aaaqaqccat tctcctgaag aaatggcaaa aacttcatct aatgtaacaa
                                                                    1137
ttatataatg tttccctttt tgattattgc attgtatttt aatttgtgca gaatgataaa
gaatgtteet tttagaagtg tgttatgtet gtacetgtet gaagagtgae attaaaettt
                                                                    1197
gaaaggactt cactgctcct ttacgatatt ccaaatagtt ttttacattg gaaaaactaa
                                                                    1257
ttcttgggat tctttcatac attttcatca aaactttcag tgtgattatg tattcatatc
                                                                    1317
                                                                    1377
ttcagtttaa tatgtcagta taatagatat tgttcaaaag tttcttgttg ctaaagtggt
gtaatctgtt acacagatga atagctagat gtggaaagag atatgtaaac aagaaacctt
                                                                    1437
tgggtattgt ttcttaagta aatattggga caatcatggt aagcaaactt agttctgtaa
                                                                     1497
ctgcattttt caccttaaaa gttaaatgaa atgcatgatg gtattttatt ccttgaatta
                                                                     1557
tgcaatgcaa cattttacat gtaaatagca ctggtcatat actgatgtat atggttatct
                                                                     1617
gggttatate tatttttatg taaactetat ttttgttttt ggcaagaagt gaaattgaga
                                                                     1677
                                                                     1737
cttatgtgca ggttgccatt gaattttgct ctggtgaatg ctgagatcca gctttttctt
                                                                     1777
acaaataaat qqqaccctgt tttccaaaaa aaaaaaamcm
<210> 270
<211> 970
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 12..497
<221> sig_peptide
<222> 12..104
<223> Von Heijne matrix
      score 5.5
      seq LVGVLWFVSVTTG/PW
<221> polyA_signal
<222> 935..940
<221> polyA_site
<222> 955..967
```

aggiciocaa g aig gog god god igg dog tot ggi dog kei get dog gag

ged gtg acg ged aga etc gtt ggt gtd etg tgg ttd gtd tda gtd act Ala Val Thr Ala Arg Leu Val Gly Val Leu Trp Phe Val Ser Val Thr

-30

Met Ala Ala Arp Pro Ser Gly Pro Xaa Ala Pro Glu -25

```
-10
aca gga coc tgg ggg got gtt goc acc toc gcc ggg ggc gag gag tcg
                                                                     146
Thr Gly Pro Trp Gly Ala Val Ala Thr Ser Ala Gly Gly Glu Glu Ser
ctt aag tgc gag gac ctc aaa gtg gga caa tat att tgt aaa gat cca
                                                                     194
Leu Lys Cys Glu Asp Leu Lys Val Gly Gln Tyr Ile Cys Lys Asp Pro
                    20
                                        25
aaa ata aat gac gct acg caa gaa cca gtt aac tgt aca aac tac aca
                                                                      242
Lys Ile Asn Asp Ala Thr Gln Glu Pro Val Asn Cys Thr Asn Tyr Thr
                35
                                    40
                                                        45
get cat gtt tee tgt ttt eea gea eee aac ata act tgt aag gat tee
                                                                      290
Ala His Val Ser Cys Phe Pro Ala Pro Asn Ile Thr Cys Lys Asp Ser
                               55
            50
agt ggc aat gaa aca cat ttt act ggg aac gaa gtt ggt ttt ttc aag
                                                                      338
Ser Gly Asn Glu Thr His Phe Thr Gly Asn Glu Val Gly Phe Phe Lys
                            70
                                                75
                                                                      386
ccc ata tct tgc cga aat gta aat ggc tat tcc tac aat gag cag tcg
Pro Ile Ser Cys Arg Asn Val Asn Gly Tyr Ser Tyr Asn Glu Gln Ser
                        85
cat gtc tct ttt tct tgg atg gtt ggg agc aga tcg att tta cct tgg
                                                                      434
His Val Ser Phe Ser Trp Met Val Gly Ser Arg Ser Ile Leu Pro Trp
                    100
                                        105
                                                                      482
ata ccc tgc ttt ggg ttt gtt aaa btt tyg cac tgt agg gtt tkg tgg
Ile Pro Cys Phe Gly Phe Val Lys Xaa Xaa His Cys Arg Val Xaa Trp
                                    120
                115
                                                                      537
aat tgg gag cct aat tgatttcaty cttatttcaa tgcagattgt tggaccttca
Asn Trp Glu Pro Asn
            130
aatggaagta gttacattat agattactat ggaaccagac ttacaagact gagtattact
                                                                      597
aatgaaacat ttagaaaaac gcaattatat ccataaatat tttttaaaag aaacagattt
                                                                      657
                                                                      717
gagcctcctt gattttaata gagaacttct agtgtatgga tttaaagatt tctctttttc
attcatatac cattttatga gttctgtata attttttgtg gtttttgttt tgttgagtta
                                                                      777
aagtatatta ttgtgagatt tatttaatag gacttccttt gaaagctgta taatagtgtt
                                                                      837
tctcgggctt ctgtctctat gagagatagc ttattactct gatactcttt aatcttttac
                                                                      897
aaaggcaagt tgccacttgt catttttgtt tctgaaaaat aaaagtataa cttattcaca
                                                                      957
                                                                      970
aaaaaaaaa mms
```

<210> 271

<211> 645

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 90..383

<221> sig_peptide

<222> 90..200

<223> Von Heijne matrix score 4.90000009536743 seq MLIMLGIFFNVHS/AV

<221> polyA_signal

<222> 609..614

<221> polyA_site

<222> 632..643

atototgooc cootgogagg goatcotggg otttotocca cogetitocg agoocgottg

WO 99/31236 -193- PCT/IB98/02122

caccteggeg atcccegact ecettett atg geg teg etc etg tge tgt ggg Met Ala Ser Leu Leu Cys Cys Gly -35 -30	113
ccg aag ctg gcc gcc tgc ggc atc gtc ctc agc gcc tgg gga gtg atc Pro Lys Leu Ala Ala Cys Gly Ile Val Leu Ser Ala Trp Gly Val Ile -25 -20 -15	161
atg ttg ata atg ctc gga ata ttt ttc aat gtc cat tcc gct gtg ttg Met Leu Ile Met Leu Gly Ile Phe Phe Asn Val His Ser Ala Val Leu -10 -5 1	209
att gag gac gtt ccc ttc acg gag aaa gat ttt gag aac ggc ccc car Ile Glu Asp Val Pro Phe Thr Glu Lys Asp Phe Glu Asn Gly Pro Gln 5 10	257
aac ata tac aac ctt tac rag caa ktc agc tac aac tgt ttc atc gct Asn Ile Tyr Asn Leu Tyr Xaa Gln Xaa Ser Tyr Asn Cys Phe Ile Ala 20 25 30	305
gca ggc ctt tac ctc ctc ctc gga ggc ttc tct ttc tgc caa ktt cgg Ala Gly Leu Tyr Leu Leu Gly Gly Phe Ser Phe Cys Gln Xaa Arg 40 45	353
ctc aat aag cgc aag gaa tac atg gtg cgc tagggccccg gcgcgtttcc Leu Asn Lys Arg Lys Glu Tyr Met Val Arg 55	403
cegetecage ecetecteta titaaaract ecetgeaceg tkteacecag gregegtece accettgeeg gegecetetg tgggactggg titeceggge rararactga atcectiete ceatetetgg cateeggece cegtggarar ggetgagget ggggggetgt teegtetete caccettege tgtgteecgt ateteaataa agagaatetg etetetteaa aaaaaaaaaa	463 523 583 643 645
<210> 272 <211> 773 <212> DNA <213> Homo sapiens	
<221> CDS <222> 332541	
<pre><221> sig_peptide <222> 332376 <223> Von Heijne matrix</pre>	
<221> polyA_signal <222> 739744	
<221> polyA_site <222> 761773	
<400> 272 aaaacaattc atgcctttca tagtttatta ttattaaagt ctaaacaaaa ttgcaatttc ttaggtaacc ttatattac aataaatgaa gattaccctc aaatgctaga agctgtctag gtccgtccgg tgtgtcagat ttcctcaga ttagatgtgc caataaccaa gttattcag taaacaactt gtacttgtt catctggttt tattactctc acccataaac agtaatgact ctctgaccct ctggaaatat gtaatgcttc caatcttgct ttgtgtatct catttaattt gttataaggt agtactgatt ttagcatatt a atg cga ttt ctt cct tgt tgt Met Arg Phe Leu Pro Cys Cys -15	60 120 180 240 300 352
ttg ctt tgg tct gtg ttc aat cca gag agc tta aat tgt cat tat ttt Leu Leu Trp Ser Val Phe Asn Pro Glu Ser Leu Asn Cys His Tyr Phe	400

•	
ghk ndd gaa amc tgt att tit gyt agt tia caa tat tat gaa att toa	448
Xaa Xaa Glu Xaa Cys Ile Phe Xaa Ser Leu Gln Tyr Tyr Glu Ile Ser	
10 15 20	
ctt cag gag aaa ctg ctg ggc ttc ctg tgg ctt tgt ttt ctt agt tac	496
Leu Gln Glu Lys Leu Leu Gly Phe Leu Trp Leu Cys Phe Leu Ser Tyr	
25 30 35 40	
	541
ttt ttc cgt gcc gtg tat ttt tta att gat ttt tct tct ttt act	341
Phe Phe Arg Ala Val Tyr Phe Leu Ile Asp Phe Ser Ser Phe Thr	
45 50 55	
tgaaaagaaa gtgttttatt ttcaaatctg gtccatattt acattctagt tcagagccaa	601
gccttaaact gtacagaatt tccactgtaa ttaaaactat ttagtgttag ttataaatag	661
ccttcaaaaa gagagattct ccattacacg atcacctgca tcacagccca tggtgaatgt	721
atgtttctgc atagcqaaat aaaaatggca aatgcactga aaaaaaaaaa aa	773
<210> 273	
<211> 566	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 43222	
<221> sig_peptide	
<222> 43177	
<223> Von Heijne matrix	
score 4	
seq ENFLSLLSKSCSA/DP	
<221> polyA_signal	
<222> 530535	
<221> polyA_site	
<222> 555566	
<400> 273	
aacgagtgga ggtgtggcta gtggctgtga tgagataaat cc atg cat agc ctt	54
Met His Ser Leu	
-45	
•	102
ttc att gcg agc ttg aaa gtt ctt ttc tat tac agt ttt agc ttt agg	102
Phe Ile Ala Ser Leu Lys Val Leu Phe Tyr Tyr Ser Phe Ser Phe Arg	
-40 -35 -30	
ttt aat tgg ttc gac tgc ctt ctc cac aat ttg ggc gag aat ttc ctt	150
Phe Asn Trp Phe Asp Cys Leu Leu His Asn Leu Gly Glu Asn Phe Leu	
-25 -20 -15 -10	
age ett ete age aaa agt tgt tet geg gae eeg tet ggg tea aet tte	198
Ser Leu Leu Ser Lys Ser Cys Ser Ala Asp Pro Ser Gly Ser Thr Phe	
	252
atg agg gac att gag aca aac aaa tgaaatatgg gttaaagtac tctgagcagc	232
Met Arg Asp Ile Glu Thr Asn Lys	
10 15	_
tacaaaaaga araccagtot atcotgotgg agacagtggo cacgtgaara aagagotott	312
gcagtatgaa agaccacatg gaaagagag ccacatggaa ccaacagtca gcatcttggt	372
ttcggacacg tgaaraaatt catctcarac tgtgtatcct aaatcaggca cttgctgaat	432
ctaactacat gagtgagacc agttgacaac acatggagca racatgagct gttctcagtg	492
chadulate yayiyayati ayiiyataat ataiyyayta rataigayay yittiinin	552
artectacae aaatteetga eteacaacae tgtgageaat aaaatggttg ttattttaag	566
ccaaaaaaaa aaaa	200

60

117

165

261

321

381 441

455

```
<210> 274
<211> 455
<212> DNA
<213 > Homo sapiens
<220>
<221> CDS
<222> 115..231
<221> sig_peptide
<222> 115..180
<223> Von Heijne matrix
      score 5
      seq HLFVTWSSQRALS/HP
<221> polyA_signal
<222> 419..424
<221> polyA site
<222> 445..455
<400> 274
aacctgccag tkatgcaaat gccaaaatgt gggtcatcat atagtatatt tgaaaccttt
ctgaacatgt acaccacca atgctagagg ctgacttgga aaccggtggg tgca atg
ccc gag gct gtg gaa caa tca gcc cat ctc ttt gtg acc tgg agc agt
Pro Glu Ala Val Glu Gln Ser Ala His Leu Phe Val Thr Trp Ser Ser
                                             -10
                         -15
    -20
cag agg gcc ctc agt cac ccc gcc cca ttc ctc acc ara raa aar aat
Gln Arg Ala Leu Ser His Pro Ala Pro Phe Leu Thr Xaa Xaa Lys Asn
                                    5
                                                         10
                    1
cca ttt cta tgg aag ctc tgacgtaact tcagtgtttt ctacaatact
Pro Phe Leu Trp Lys Leu
             15
cetectgece egececatta aaacagttet tttgttaaaa aataveetaa tggtecaact
ttgctgtctg ttcttccaaa tgtttataat acacattatt tataaatatg tctgtttggg
 aagctaagaa caagctagtt tttacaacac aaatggaaat aaatgcaatt attataaaaa
 tycaaaaaaa aaaa
 <210> 275
 <211> 673
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> CDS
 <222> 232..384
 <221> sig_peptide
 <222> 232..300
 <223> Von Heijne matrix
       score 3.70000004768372
       seq FFLCAAFPLGAGV/KM
 <221> polyA_signal
```

<222> 650..655

<221> polyA_site <222> 662..673

<400> 275	
atttggettg cagactgeet tetateceag aacagetgag aaatetatga agetgagatt	60
ctgaaggace cagettaggt tettecaett aggeeteaat teeetteett ttecagggge	120
agentiaget teccatgged etgaaacaca cacattteed cetteettte ceagaageca	180
ctggccccc atagcaccca gtgcatectt tttacaagtg gaagaactag g atg gct	237
Met Ala	
tto caa agt ott cta gaa atg aag tto ttt oto tgt goa got tto coo	285
Phe Gln Ser Leu Leu Glu Met Lys Phe Phe Leu Cys Ala Ala Phe Pro	
-20 -15 -10	
ctt gga gca gga gtg aag atg ttt cat tat ctt ggg cct ggg aaa cca	333
Leu Gly Ala Gly Val Lys Met Phe His Tyr Leu Gly Pro Gly Lys Pro	
-5 1 5 10	
ctt cyy cag get tet eec tee eec cae eec cat agg ame agg att tgg	381
Leu Xaa Gln Ala Ser Pro Ser Pro His Pro His Arg Xaa Arg Ile Trp	
15 20 25	
cet tagettetgg geetatesge tgeetteeet ettytteeta ceacetette	434
Pro	
tgccttcctt trawctctgt tgggcttggg gatcttagtt ttcttttgtt tatctccat	494
ctcatttttt tottotggto agtttttta agggggggtg ttgtggtttt ttgtttttgt	554
tttgcttctg aaaaarcatt tgcctttctt cctctcccaa cataacaatc gtggtaacag	614
aatgcgactg ctgatttacc gatgtattta atgtaagtaa aaaaaggaaa aaaaraaaa	673
aatgegactg etgatetact gatgeateta degeadgeda dadaagged bestelling	
222	
<210> 276	
<211> 639	
<212> DNA	
<213> Homo sapiens.	
<220>	
<221> CDS	
<222> 143427	
<221> sig_peptide	
<222> 143286	
<223> Von Heijne matrix	
score 7.5	
seq FVILLLFIFTVVS/LV	
-	
<221> polyA signal	
<222> 606611	
<221> polyA site	
<222> 628639	
<400> 276	
aatcgcttca gcagcatcct ctcagacaag agccactatt tctgattcag atcacctgtc	60
atcgaagttt aaagaagggg aaacaggaga cagaaataca ctgaaccaaa aagattcaaa	120
agagcaagtg gaatetetaa ga atg get tee age cae tgg aat gaa ace act	172
Met Ala Ser Ser His Trp Asn Glu Thr Thr	
-45 -40	
ace tet gtt tat cag tae ett ggt ttt caa gtt caa aaa att tae eet	220
Thr Ser Val Tyr Gln Tyr Leu Gly Phe Gln Val Gln Lys Ile Tyr Pro	
-A -7E	
	268
tte cat gae aac tgg aac act gee tge ttt gte ate etg ett tta ttt	
Phe His Asp Asn Trp Asn Thr Ala Cys Phe Val Ile Leu Leu Phe	
-20 -15 -10 Gaa grg	316
ata ttt aca gtg gta tct tta gtg gtg ctg gct ttc ctt tat gaa gtg	210
Ile Phe Thr Val Val Ser Leu Val Val Leu Ala Phe Leu lyr Giu Val	
-5 · 1 5 · 10	264
ctt gam wgc tgc tgc tgt gta aaa aac aaa acc gtg aaa gac ttg aaa	364
Leu Xaa Xaa Cys Cys Cys Val Lys Asn Lys Thr Val Lys Asp Leu Lys	

15 20 25	
agt gaa ccc aac cct ctt ara akt atg atg gac aac atc aga aaa cgt	412
Ser Glu Pro Asn Pro Leu Xaa Xaa Met Met Asp Asn Ile Arg Lys Arg 30 35 40	
30 35 40 gaa act gaa gtg gtc taacactcta taraaaatga acaaaatctc tgaaagcagc	467
Glu Thr Glu Val Val	40,
45	
tcaacctctt ctgaraaaaa aaatatattc tgaggccaac tgttgctaca aaacaaattc	527
tgactgaatg gttaaaacat ttctagtara aggggaaaaa aaakttaaac atgcactgtt	587
tgtgtgtata sccatttcat taaatataca gtaaaactyc aaaaaaaaaa aa	639
<210> 277	
<211> 772 <212> DNA	
<213> Homo sapiens	
2213) nomo sapiem	
<220>	
<221> CDS	
<222> 284463	
<221> sig_peptide	
<222> 284379	
<223> Von Heijne matrix	
score 3.79999995231628	
seq TFINITLWLGSLC/QR	
<221> polyA_site	
<222> 762772	
<400> 277	
acagetgggg ctttgtcttc tttattgcta ggagaatgta gcaatagaag ttctcatcgc	60
cctgtattgc acttttggtt ttaaggactg gacccagagt tcctgaaagc caaactccat	120
aagetgetea gtaagtteea ageacatage eggetkhggg atgegatteg gtegaggtet	180
gttgaatgaa ggtagacgca gcaggcagtt tgtccttacc agtgacctgg aagacggtgg	240 295
cacttcctga gtgagctcac ttaccttccc tgaatggtga ggc atg gat gaa tat Met Asp Glu Tyr	233
-30	
tee tgg tgg tge cae gtg tta gag gtg gta aag ggt caa atg ttt act	343
Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr	
-25 -20 -15	
ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt ttc	391
Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe	
-10 -5 1	
tat god tog ggt act tat tto ota ata tat ato ago aca gta acg cot	439
Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro	
5 10 15 20	
age tgg agg ett tgt ett gtt agt tgataaatta gtggtaacag gtagatttgg	493
Ser Trp Arg Leu Cys Leu Val Ser	
25	553
ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct	61:
tttgaaagag agaagtetee etgtgttgeg caggetggte teagacteet ggggteaagt	67
gageeteetg etttegeete etaaagtget gggattaeag gegtgageea eegeaceegg acagatgtgt tgattttaaa gtgggtatga ggeetgagee etggagtttg agaceageet	73
ggacaacatg gcaagaccct gtctctccaa aaaaaaaaa	77
Adactacaca Acaadacce Accessona anananan	

<210> 278

<211> 840

<212> DNA

```
<213> Homo sapiens
<220>
<221> CDS
<222> 162..671
<221> sig_peptide
<222> 162..398
<223> Von Heijne matrix
     score 4.09999990463257
     seq QGVLFICFTCARS/FP
<221> polyA_signal
<222> 805..810
<221> polyA site
<222> 830..840
<400> 278
aaaaactgag gcctgggagc aggaacctgt aggcagcgct tgagggtagc gggatagcag
                                                                     60
                                                                     120
ctgcaacgcg cgtgggaggc gggggctctg ggcggaacaa aaatcacagg atgtcagagg
atgtttcccg ggaagaactg ggataaaggg gtcccagcac c atg gag gac ccg aac
                                              Met Glu Asp Pro Asn
cct gaa gag aac atg aag cag cag gat tca ccc aag gag aga agt ccc
                                                                     224
Pro Glu Glu Asn Met Lys Gln Gln Asp Ser Pro Lys Glu Arg Ser Pro
                                    -65
                -70
cag ago coa gga ggo aac ato tgo cao otg ggg goo cog aag tgo acc
                                                                     272
Gln Ser Pro Gly Gly Asn Ile Cys His Leu Gly Ala Pro Lys Cys Thr
                                -50
                                                    -45
           -55
ege tge etc atc ace tte gea gat tee aag tte eag gag egt eac atg
Arg Cys Leu Ile Thr Phe Ala Asp Ser Lys Phe Gln Glu Arg His Met
                            -35
aag cgg gag cac cca gcg gac ttc gtg gcc cag aag ctg cag ggg gtc
                                                                     368
Lys Arg Glu His Pro Ala Asp Phe Val Ala Gln Lys Leu Gln Gly Val
                                            -15
                        -20
ete tte ate tge tte ace tge gee ege tee tte ece tee tee aaa gee
Leu Phe Ile Cys Phe Thr Cys Ala Arg Ser Phe Pro Ser Ser Lys Ala
                                        1
-10
                    -5
ckr rkc acc cac car cgc agc cac ggt cca rcc gcc aag ccc acc ctg
                                                                      464
Xaa Xaa Thr His Gln Arg Ser His Gly Pro Xaa Ala Lys Pro Thr Leu
                                                    20
cog gtt gca acc act act gcc car ccc acc ttc cct tgt cct gac tgt
                                                                      512
Pro Val Ala Thr Thr Thr Ala Gln Pro Thr Phe Pro Cys Pro Asp Cys
                                                35
                            30
ggc aaa acc ttt ggg cag gct gtt tct ctg arg cgg cac csc caa atr
                                                                      560
Gly Lys Thr Phe Gly Gln Ala Val Ser Leu Xaa Arg His Xaa Gln Xaa
                        45
                                            50
cat gar gtc egt gec eet eet ggc ace ttc gec tgc aca rad tgc ggt
                                                                      608
His Glu Val Arg Ala Pro Pro Gly Thr Phe Ala Cys Thr Xaa Cys Gly
                    60
                                         65
cag gac tit gct car gaa rca ggg ctg cat caa cac tac att cgg cat
                                                                      656
Gln Asp Phe Ala Gln Glu Xaa Gly Leu His Gln His Tyr Ile Arg His
                                    80
                75
gee egg ggg gga ete tgagtteage ttaageetet ceaeggtgae gggtggetet
                                                                      711
Ala Arg Gly Gly Leu
            90
gtggctggta ggactcaccc atgatatggg gtgcaggaac tctgggggcc ctgaaggatt
                                                                       771
                                                                       831
tgetteecte ecctgggaag geagaggget ettaataaag aggacecaka agattettaa
                                                                       840
aaaaaaaa
```

WO 99/31236 -199- PCT/IB98/02122

```
<210> 279
<211> 840
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 63..632
<221> sig_peptide
<222> 63..308
<223> Von Heijne matrix
      score 4.40000009536743
      seq NLPHLQVVGLTWG/HI
<221> polyA_signal
<222> 808..813
<221> polyA site
<222> 829..840
<400> 279
aacttceggt cgcgccascg cccgttgcca gttctgcgcg tgtcctgcat ctccagtatg
                                                                     60
ga atg tat gtd tgg ccc tgt gct gtg gtc ctg gcc cag tac ctt tgg
                                                                    107
   Met Tyr Val Trp Pro Cys Ala Val Val Leu Ala Gln Tyr Leu Trp
                               -75
ttt cac aga aga tot otg oca ggo aag goo ato tta gag att gga got
                                                                     155
Phe His Arg Arg Ser Leu Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala
                  -60
                                            -55
gga gtg agc ctt cca gga att ttg gct gcc aaa tgt ggt gca gaa gta
                                                                     203
Gly Val Ser Leu Pro Gly Ile Leu Ala Ala Lys Cys Gly Ala Glu Val
                                            -40
                        -45
ata ctg tca gac age tca gaa ctg cct. cae tgt ctg gaa gtc tgt cgg
                                                                     251
Ile Leu Ser Asp Ser Ser Glu Leu Pro His Cys Leu Glu Val Cys Arg
                                    - -25
                    -30
                                                                     299
caa age tge caa atg aat aac etg eca cat etg cag gtg gta gga eta
Gln Ser Cys Gln Met Asn Asn Leu Pro His Leu Gln Val Val Gly Leu
                                    -10
                -15
                                                                     347
aca tgg ggt cat ata tet tgg gat ett etg get eta eca eca caa gat
Thr Trp Gly His Ile Ser Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp
                            5
att atc ctt gca tct gat gtg ttc ttt gaa cca gaa rat ttt gaa gac
                                                                     395
Ile Ile Leu Ala Ser Asp Val Phe Phe Glu Pro Glu Xaa Phe Glu Asp
                                            25
                        20
att ttg gct aca ata tat ttt ttg atg cac aar aat ccc aag gtc caa
                                                                      443
Ile Leu Ala Thr Ile Tyr Phe Leu Met His Lys Asn Pro Lys Val Gln
                     35
                                        40
                                                                      491
 ttg tgg tct act tat caa gtt agg art gct gac tgg tca ctt gaa gct
 Leu Trp Ser Thr Tyr Gln Val Arg Xaa Ala Asp Trp Ser Leu Glu Ala
                                     55
 tta ctc tac aaa tgg gat atg aaa tgt gtc cac att cct ctt gag tct
                                                                      539
 Leu Leu Tyr Lys Trp Asp Met Lys Cys Val His Ile Pro Leu Glu Ser
                                 70
             65
 ttt gat gca gac aaa gaa rat ata gca gaa tct acc ctt cca gga aga
                                                                      587
 Phe Asp Ala Asp Lys Glu Xaa Ile Ala Glu Ser Thr Leu Pro Gly Arg
                             85
 cat aca gtt gaa atg ctg gtc att tcc ttt gca aag gac agt ctc
                                                                      632
 His Thr Val Glu Met Leu Val Ile Ser Phe Ala Lys Asp Ser Leu
                                             105
                         100
 tgaattatac ctacaacctg ttctgggaca gtatcaatac tgatgagcaa cctggcacac
                                                                      692
 aaactatgag cagaccactt cagcttgaga atgcagtggg tctgaagatg gtcaagtctg
                                                                      752
```

812

tttgccttar attttgatgt cacctagaca acacttaaac tcatatgaaa caaaaattaa aatacqtatt acaagcaaaa aaaaaaaa 840 <210> 280 <211> 849 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 21..362 <221> sig_peptide . <222> 21..200 <223> Von Heijne matrix score 4.80000019073486 seq LVILSLKSQTLDA/ET <221> polyA_signal <222> 821..826 <221> polyA site <222> 838..849 <400> 280 agtaagteec ecceectege atg atg get geg gtg eeg eeg gge etg gag eeg 53 Met Met Ala Ala Val Pro Pro Gly Leu Glu Pro -60 -55 tgg aac cgt gtg aga atc cct aag gcg ggg aac cgc agc gca gtg aca 101 Trp Asn Arg Val Arg Ile Pro Lys Ala Gly Asn Arg Ser Ala Val Thr -35 -45 -40 gtg cag aac cee gge geg gee ett gae ett tge att gea get gta att 149 Val Gln Asn Pro Gly Ala Ala Leu Asp Leu Cys Ile Ala Ala Val Ile -30 -25 -20 aaa gaa tgc cat ctc gtc ata ctg tcg ctg aag agc caa acc tta gat 197 Lys Glu Cys His Leu Val Ile Leu Ser Leu Lys Ser Gln Thr Leu Asp -15 -10 245 gca gaa aca gat gtg tta tgt gca gtc ctt tac agc aat cac aac aga Ala Glu Thr Asp Val Leu Cys Ala Val Leu Tyr Ser Asn His Asn Arg 5 10 293 atg ggc cgc cac aaa ccc cat ttg gcc ctc aaa cag gtt gag caa tgt Met Gly Arg His Lys Pro His Leu Ala Leu Lys Gln Val Glu Gln Cys 20 25 tta aag cgt ttg aaa aac atg aat ttg gag ggc tca att caa gac ctg 341 Leu Lys Arg Leu Lys Asn Met Asn Leu Glu Gly Ser Ile Gln Asp Leu 40 392 ttt gag ttg ttt tct tcc aag taagtaagtg gtccarttgc tttgtgatgt Phe Glu Leu Phe Ser Ser Lys 50 ggtgggctgg gaactcaatg tottgtgatc kcccttwgga ttkctctakg ctygckgttg 452 512 gaatataacc aattataccw cagctgtaka aatwttgttt taatgtgggg taccyggtgt 572 ktgtggtaat cttctgacat tgatctatgg gartgactgg tgtgacattg aaatctgggt catggtagat tatattaaaa catcagtggg ctgttattgt gcttaactac ctcaagttga 632 692 gcttaaagca agtcttcact tgaaaactgc tatagaaatg ctttatattt aaaaatgaaa gtaatgggar mttgcacata gctgaaaatg tgaagggtcg cccagggagg amatggaagc 752 tetgtgette ttetgecata cettgeceta tgeatetett tgttteaate etttgteata 812 849 tcctttataa taaactggta aatgtaaaaa aaaaaaa

```
<210> 281
<211> 1344
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 21..503
<221> sig peptide
<222> 21..344
<223> Von Heijne matrix
      score 5.30000019073486
      seq ACMTLTASPGVFP/SL
<221> polyA signal
<222> 1305..1310
<221> polyA site
<222> 1330..1341
<400> 281
aaacaactcc ggaaagtaca atg acc agc ggg cag gcc cga gct tcc wyc cag
                      Met Thr Ser Gly Gln Ala Arg Ala Ser Xaa Gln
                                  -105
                                                      -100
tee eec cag gee etg gag gae teg gge eeg gtg aat ate tea gte tea
                                                                     101
Ser Pro Gln Ala Leu Glu Asp Ser Gly Pro Val Asn Ile Ser Val Ser
                           -90
                                               -85
atc acc cta acc ctg gac cca ctg aaa ccc ttc gga ggg tat tcc cgc
                                                                     149
Ile Thr Leu Thr Leu Asp Pro Leu Lys Pro Phe Gly Gly Tyr Ser Arg
                     -75
                                            -70
aac gtc acc cat ctg tac tca acc atc tta ggg cat cag att gga ctt
                                                                     197
Asn Val Thr His Leu Tyr Ser Thr Ile Leu Gly His Gln Ile Gly Leu
                    -60
                                        - 55
tca ggc agg gaa gcc cac gag gag ata aac atc acc ttc acc ctg cct
                                                                     245
Ser Gly Arg Glu Ala His Glu Glu Ile Asn Ile Thr Phe Thr Leu Pro
                -45
                                    -40
aca gcg tgg agc tca gat gac tgc gcc ctc cac ggt cac tgt gag cag
                                                                     293
Thr Ala Trp Ser Ser Asp Asp Cys Ala Leu His Gly His Cys Glu Gln
                                -25
gtg gta ttc aca gcc tgc atg acc ctc acg gcc acc cct ggg gtg ttc
Val Val Phe Thr Ala Cys Met Thr Leu Thr Ala Ser Pro Gly Val Phe
        -15
                            -10
ccg tca ctg tac agc cac cgc act gtg ttc ctg aca cgt aca gca acg
                                                                     389
Pro Ser Leu Tyr Ser His Arg Thr Val Phe Leu Thr Arg Thr Ala Thr
                                        10
cca cgc tct ggt aca aga tct tca caa ctg cca gag atg cca aca caa
                                                                     437
Pro Arg Ser Gly Thr Arg Ser Ser Gln Leu Pro Glu Met Pro Thr Gln
                20
aat acg ccc aaa att aca atc ctt tct ggt gtt ata agg ggg cca ttg
                                                                     485
Asn Thr Pro Lys Ile Thr Ile Leu Ser Gly Val Ile Arg Gly Pro Leu
           35
                               40
                                                    45
gaa aag tot atc atg ott taaatoocaa gottacagtg attgttccag
                                                                     533
Glu Lys Ser Ile Met Leu
atgatgaccg ttcattaata aatttgcatc tcatgcacac cagttacttc ctctttgtga
                                                                     593
tggtgataac aatgttttgc tatgctgtta tcaagggcag acctagcaaa ttgcgtcaga
                                                                      653
gcaatcotga attitigtoco gagaaggtgg ottitiggotga agostaatto sacagotoot
tgttttttga gagagactga gagaaccata atocttgcct gctgaaccca gcctgggcct
                                                                     773
ggatgctctg tgaatacatt atcttgcgat gttgggttat tccagccaaa gacatttcaa
                                                                     833
                                                                     893
gtgcctgtaa ctgatttgta catatttata aaaatctatt cagaaattgg tccaataatg
                                                                      953
cacgtgcttt gccctgggta cagccagage cettcaacce cacettggae ttgaggaeet
```

acctgatggg acgtttccac gtgtctctag agaaggatcc tggatctagc tggtcacgac

1013

```
ttcttgtttc agcccaatat gtagagaaca tttgaaacag tctgcacctt tgatacggta
                                                                1133
ttgcatttcc aaagccacca atccattttg tggattttat gtgtctgtgg cttaataatc
                                                                1193
atagtaacaa caataatacc tttttctcca ttttgcttgc aggaaacata ccttaagttt
                                                                1253
1313
gtcacatttt aatacyaaaa aaaaaaaamc h
                                                                1344
<210> 282
<211> 671
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 1..201
<221> sig peptide
<222> 1..63
<223> Von Heijne matrix
     score 5.09999990463257
     seq LLLKIWLLQRPES/QE
<221> polyA signal
<222> 637..642
<221> polyA_site
<222> 660..671
<400> 282
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt
                                                                 48
Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu
                      -15
                                         -10
caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg
                                                                 96
Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val
                  1
atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt
                                                                144
Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val
           15
                              20
ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca
                                                                 192
Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro
       30
                          35
                                             40
ctt agg atg tgatcacttt caggtggcca ggaatgttga atgtctttgg
                                                                 241
Leu Arg Met
   45
ctcagttcat ttaaaaaaga tatctatttg aaagttctca rarttgtaca tatgtttcac
agtacaggat ctgtacataa aagtttcttt cctaaaccat tcaccaagag ccaatatcta
                                                                 361
ggcattttct tggtagcaca aattttctta ttgcttaraa aattgtcctc cttgttattt
                                                                 421
ctgtttgtaa racttaagtg agttaggtct ttaaggaaag caacgctcct ctgaaatgct
                                                                 481
tgtctttttt ctgttgccga aatarctggt cctttttcgg gagttaratg tatarartgt
                                                                 541
ttgtatgtaa acatttcttg taggcatcac catgaacaaa gatatattt ctatttattt
                                                                 601
attatatgtg cacttcaaga agtcactgtc agagaaataa agaattgtct taaatgtcaa
                                                                 661
aaaaaaaaa
                                                                 671
```

<210> 283

<211> 1601

<212> DNA

<213> Homo sapiens

```
<220>
<221> CDS
<222> 39..1034
<221> sig_peptide
<222> 39..134
<223> Von Heijne matrix
     score 6.09999990463257
     seq LPLLTSALHGLQQ/QH
<221> polyA_signal
<222> 1566..1571
<221> polyA_site
<222> 1587..1597
agececagat cetgaaggag gtgcagagee cagagggg atg ate keg etg agg gae
                                                                      56
                                          Met Ile Xaa Leu Arg Asp
                                                  -30
aca gct gcc tcc ctc cgc ctt gag aga gac aca agg cag ttg cca ctg
                                                                     104
Thr Ala Ala Ser Leu Arg Leu Glu Arg Asp Thr Arg Gln Leu Pro Leu
                        -20
                                            -15
ctc acc agt gcc ctg cac gga ctg cag cag cac cca gcc ttc tct
                                                                     152
Leu Thr Ser Ala Leu His Gly Leu Gln Gln Gln His Pro Ala Phe Ser
                   -5
                                       1
ggt gtg gca cgg ctg gcc aag cgg tgg gtg cgt gcc cag ctt ctt ggt
                                                                     200
Gly Val Ala Arg Leu Ala Lys Arg Trp Val Arg Ala Gln Leu Leu Gly
                               15
gag ggt ttc gct gat gag agc ctg gat ctg gtg gcc gct gcc ctt ttc
                                                                     248
Glu Gly Phe Ala Asp Glu Ser Leu Asp Leu Val Ala Ala Ala Leu Phe
                           30
                                                                     296
ctg cac cct gag ccc ttc acc cct ccg agt tcc ccc cag gtt ggc ttc
Leu His Pro Glu Pro Phe Thr Pro Pro Ser Ser Pro Gln Val Gly Phe
                        45
ctt cga ttc ctt ttc ttg gta tca acg ttt gat tgg aag aac aac ccc
                                                                     344
Leu Arg Phe Leu Phe Leu Val Ser Thr Phe Asp Trp Lys Asn Asn Pro
                                        65
                    60
ctc ttt gtc aac ctc aat aat gag ctc act gtg gag gag cag gtg gar
Leu Phe Val Asn Leu Asn Asn Glu Leu Thr Val Glu Glu Gln Val Glu
                                    80
ate ege agt gge tte etg gea get egg gea eag ete eee gte atg gte
                                                                      440
Ile Arg Ser Gly Phe Leu Ala Ala Arg Ala Gln Leu Pro Val Met Val
                                95
            90
att gtt acc ccc caa rac cgc aaa aac tct gtg tgg aca cag gat gga
                                                                      488
Ile Val Thr Pro Gln Xaa Arg Lys Asn Ser Val Trp Thr Gln Asp Gly
                            110
                                                115
ccc tca gcc car atc ctg cag cag ctt gtg gtc ctg gca gct gaa scc
                                                                      536
Pro Ser Ala Gln Ile Leu Gln Gln Leu Val Val Leu Ala Ala Glu Xaa
                        125
                                            130
                                                                      584
ctq ccc atq tta rar aas cag ctc atg gat ccc cgg gga cct ggg gac
Leu Pro Met Leu Xaa Xaa Gln Leu Met Asp Pro Arg Gly Pro Gly Asp
                   140
                                        145
atc agg aca gkg ttc egg eeg eec ttg gae att tae gae gtg etg att
                                                                      632
Ile Arg Thr Xaa Phe Arg Pro Pro Leu Asp Ile Tyr Asp Val Leu Ile
                                    160
                155
ege etg tet eet ege eat ate eeg egg eac ege eag get gtg gae ter
                                                                      680
Arg Leu Ser Pro Arg His Ile Pro Arg His Arg Gln Ala Val Asp Ser
                                175
            170
                                                                      728
cca got god too too tgc egg ggd etg etc age eag eeg ggg eec tea
Pro Ala Ala Ser Phe Cys Arg Gly Leu Leu Ser Gln Pro Gly Pro Ser
```

185 190 195	
too otg atg occ gtg otg ggo tak gat cot cot cag oto tat otg acg	776
Ser Leu Met Pro Val Leu Gly Xaa Asp Pro Pro Gln Leu Tyr Leu Thr	
200 205 210	
cag ctc arg gag gcc ttt ggg gat ctg gcc ctt ttc ttc tat gac cag Gln Leu Xaa Glu Ala Phe Gly Asp Leu Ala Leu Phe Phe Tyr Asp Gln	824
215 220 225 230	
cat ggt gga gag gtg att ggt gtc ctc tgg aag ccc acc agc ttc cag	872
His Gly Gly Glu Val Ile Gly Val Leu Trp Lys Pro Thr Ser Phe Gln	• • •
235 240 245	
ecg cag ccc ttc aag gcc tcc agc aca aag ggg cgc atg gtg atg tct	920
Pro Gln Pro Phe Lys Ala Ser Ser Thr Lys Gly Arg Met Val Met Ser 250 255 260	
cga ggt ggg gag cta gta atg qtg ccc aat gtt gaa gca atc ctg gag	968
Arg Gly Glu Leu Val Met Val Pro Asn Val Glu Ala Ile Leu Glu	900
265 270 275	
gac ttt gct gtg ctg ggt gaa ggc ctg gtg cag act gtg gag gcc cga	1016
Asp Phe Ala Val Leu Gly Glu Gly Leu Val Gln Thr Val Glu Ala Arg	
280 285 290	
agt gag agg tgg act gtg tgatcccagc tctggagcaa gctgtagacg Ser Glu Arg Trp Thr Val	1064
295 300	
gacagcagga cattggacct ctagagcaag atgtcagtag gatgacctcc accetecttg	1124
gacatgaatc ctccatggag ggcctgctgg ctgaacatgc tgaatcatct ccaacaaaac	1184
ccagececaa etttetetet gatgetecag cattggggea ggggcatggt ggeceatgta	1244
gtotootggg cotcaccato coagaagagg agtgggagoo agotcagaga aggaactgaa	1304
cocaggagat coatcoacct attagecetg ggeetggace tecetgegat treceactee	1364
tttcttagtc ttcttccaga aacagagaag gggatgtgtg cctgggagag gctctgtctc	1424
cttcctgctg ccaggacctg tgcctagact tagcatgccc ttcactgcag tgtcaggcct	1484
ttagatggga cccagcgaaa atgtggccct tctgagtcac atcaccgaca ctgagcagtg gaaaggggct atatgtgtat gaatagacca cattgaagga gcaaaaaaaa aaamcch	1544 1601
J J J J J J J J J J J J J J J J	1001
The second of th	1001
	1001
<210> 284	1001
<210> 284 <211> 1206	1001
<210> 284 <211> 1206 <212> DNA	1001
<210> 284 <211> 1206	1001
<210> 284 <211> 1206 <212> DNA	1001
<210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS	1001
<210> 284 <211> 1206 <212> DNA <213> Homo sapiens	1001
<210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263	1001
<210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig peptide	1001
<210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125	1001
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix score 3.90000009536743</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens </pre> <pre><220> <221> CDS <222> 69263 </pre> <pre><221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	60
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	60
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	60
<pre><210> 284 <211> 1206 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69263 <221> sig_peptide <222> 69125 <223> Von Heijne matrix</pre>	60 110

-5 1 5 10	
aga cac cac ata ctg cag cag ttc cta gtg aga aaa tct gtg cca cta	206
Arg His His Ile Leu Gln Gln Phe Leu Val Arg Lys Ser Val Pro Leu	200
15 20 25	
gaa aat get tea ett eea ttt eet eac etg gge agt tet etg ttt aaa	254
Glu Asn Ala Ser Leu Pro Phe Pro His Leu Gly Ser Ser Leu Phe Lys	234
30 35 40	
att gtg ggc tgatttggtc ttcctctcct cctcccactg ttactgccct	303
Ile Val Gly	303
45	
gcagcccttg trcaggtgta cagaccctta trctggcctc tagtgtcctt gtctgtcatg	363
acacaccett cegeccaaat acetetgace ccaaggetgg aatggggetg gtaggarata	423
agtitigetta eteatartea tgteetttet ettggeaeet getteeetge ggtgteetea	483
aatggatttc tgtgtggcag tggartgatt gcatgaattt ttctgtaaca cattaacttt	543
gtattattat taagggartt tgaraaagct ttgcttataa tgtcaaggca aggaggtaaa	603
aactggagcc caaakaaatt cccttagggc aagattatgt tataataraa aattgaattt	663
cctgaggcag tggctgccac cccttttcar atgtttagtc ctgcaaatag catctttctt	723
gtag_ctgtg acatggatgg ggatgctagg gcccttaggg gcaaggggac taalctaaat	783
caakttgagt ttttttccag caggggttar gggaggtact csctgttgat atttgacact	843
araaagtaat ctttttaca aaactgtttt tctaggtggg tggaaagtga aactgccaca	903
tccttgttgg tttagtccaa raratcattt gcaacaacag taratgtccg ggttttgttt	963
ctgtcttttt attatgaaaa actatgttaa gggggaaaat gtggattatg gtaaccarag	1023
gaatccctas ccttgttttc cttaraarac ttgtttagtg ttttatcara cgtctgttgt	1083
agttgtarac aggaaagctt gtgaraaaaa caccacatgg ascctgtaaa tgtttttgca	1143
caacctgtaa agcattettg gaaktggcca gtaaaaaggg gttttaccat ttaaaaaaaa	1203
aat	1206
	1200
<210> 285	
<211> 536	
<212> DNA	
<213> Homo sapiens	
·	
<220>	
<221> CDS	
<222> 115285	
<221> sig_peptide	
<222> 115204	
<223> Von Heijne matrix	
score 3.7000004768372	
seq SMMLLTVYGGYLC/SV	
<221> polyA_signal	
<222> 505510	
<221> polyA_site	
<222> 525536	
<400> 285	
acgagtgctg cgttcggctg tgctgggaag ttgcgtagac agtggcctcg agaccctgcc	60
TOCCTORIOR PROCESSORY CONTROLLED	
tgcctgagga ggcctcggtt ggatgcgaag gagctgcagc atccagggga caag atg	117
Met	
-30	
cca act ggc aag cag cta gct gac att ggc tat aag acc ttc tct acc	
Pro Thr Gly Lys Gln Leu Ala Asp Ile Gly Tyr Lys Thr Phe Ser Thr	165
	165
-25 -20 -15	
-25 -20 -15 too atg atg ott oto act gtg tat ggg ggg tac oto tgc agt gtc cga	165 213
-25 -20 -15 tcc atg atg ctt ctc act gtg tat ggg ggg tac ctc tgc agt gtc cga Ser Met Met Leu Leu Thr Val Tyr Gly Gly Tyr Leu Cys Ser Val Arg	
-25 -20 -15 tcc atg atg ctt ctc act gtg tat ggg ggg tac ctc tgc agt gtc cga Ser Met Met Leu Leu Thr Val Tyr Gly Gly Tyr Leu Cys Ser Val Arg -10 -5 1	213
-25 -20 -15 tcc atg atg ctt ctc act gtg tat ggg ggg tac ctc tgc agt gtc cga Ser Met Met Leu Leu Thr Val Tyr Gly Gly Tyr Leu Cys Ser Val Arg	

5 10 15	
gaa cag aag dac tca gga atc atg tagaactggg gggctttttc tcctgagcar Glu Gln Lys Xaa Ser Gly Ile Met 20 25	315
asakgcccaa ggcatgctgt ggagagactt cacctgccac catttccagg tcaacaggac	275
tagagegttg atggttttea aaceetgttg gaagaaagtg cecatggttt etetggttet	375 435
gccartttga cagtttatgg argettttga ategtaatar caatgtgagg gtgargtaca	495
cctacagaca ttaaataatt tgctgtgtca aaaaaaaaaa	536
The second secon	330
<210> 286	
<211> 529	
<212> DNA	
<213> Homo sapiens	
•	
<220>	
<221> CDS	
<222> 90344	
- 10-1-1 - 1	
<221> sig peptide	
<222> 90140	
<223> Von Heijne matrix	
score 8.19999980926514	
seq LLLITAILAVAVG/FP	
<221> polyA_signal ·	
<222> 500, .505	
<221> polyA_site	
<222> 515527	
<400> 286	
aatatrarac agctacaata ttccagggcc artcacttgc catttctcat aacagcgtca	60
gagagaaaga actgactgar acgtttgag atg aag aaa gtt ctc ctc ctg atc	113
Met Lys Lys Val Leu Leu Ile	
2,0 2,0 741 204 204 214	
-15 -10	
-15 -10	161
aca god ato tig god gig got giw ggt tito coa gid tot caa gad dag	161
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln	161
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 1 5	
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 1 5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr	161 209
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 1 5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly	
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 1 5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 20	209
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 20 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att	
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 20 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile	209
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 20 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 30 35	209
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 cca ttt cca aga ttt cca tgg ttt aga cgt aat ttt cct att cca ata	209
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 30 35 cca ttt cca aga ttt cca tgg ttt aga cgt aat ttt cct att cca ata Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Asn Phe Pro Ile Pro Ile	209
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 cca ttt cca aga ttt cca tgg ttt aga cgt aat ttt cct att cca ata Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Asn Phe Pro Ile Pro Ile 40 5 45 6 6 7 8 8 8 8 8 8 8 8 8 8 8 8	209 257 305
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 cca ttt cca aga ttt cca tgg ttt aga cgt aat ttt cct att cca ata Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Asn Phe Pro Ile Pro Ile 40 45 cct gaa tct gcc cct aca act ccc ctt cct agc gaa aag taaacaaraa	209
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 cca ttt cca aga ttt cca tgg ttt aga cgt aat ttt cct att cca ata Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Asn Phe Pro Ile Pro Ile 40 5 45 6 6 7 8 8 8 8 8 8 8 8 8 8 8 8	209 257 305
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 cca ttt cca aga ttt cca tgg ttt aga cgt aat ttt cct att cca ata Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Asn Phe Pro Ile Pro Ile 40 45 cct gaa tct gcc cct aca act ccc ctt cct agc gaa aag taaacaaraa	209 257 305
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 cca ttt cca aga ttt cca tgg ttt aga cgt aat ttt cct att cca ata Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Asn Phe Pro Ile Pro Ile 40 45 cct gaa tct gcc cct aca act ccc ctt cct agc gaa aag taaacaaraa Pro Glu Ser Ala Pro Thr Thr Pro Leu Pro Ser Glu Lys	209 257 305
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 cca ttt cca aga ttt cca tgg ttt aga cgt aat ttt cct att cca ata Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Asn Phe Pro Ile Pro Ile 45 cct gaa tct gcc cct aca act ccc ctt cct agc gaa aag taaacaaraa Pro Glu Ser Ala Pro Thr Thr Pro Leu Pro Ser Glu Lys 60 ggaaaagtca crataaacct ggtcacctga aattgaaatt gagccacttc cttgaaraat	209 257 305
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 cca ttt cca aga ttt cca tgg ttt aga cgt aat ttt cct att cca ata Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Asn Phe Pro Ile Pro Ile 40 45 cct gaa tct gcc cct aca act ccc ctt cct agc gaa aag taaacaaraa Pro Glu Ser Ala Pro Thr Thr Pro Leu Pro Ser Glu Lys 60 65	209 257 305 354

<210> 287 <211> 493 <212> DNA

```
<213> Homo sapiens
<220>
<221> CDS
<222> 57..311
<221> sig_peptide
<222> 57..107
<223> Von Heijne matrix
     score 8.19999980926514
      seq LLLITAILAVAVG/FP
<221> polyA signal
<222> 467..472
<221> polyA_site
                                    2050
<222> 482..493
<400> 287
aacttgccat ttctcataac agcgtcagag agaaagaact gactgaaacg tttgag atg
                                                                      59
aag aaa gtt ctc ctc ctg atc aca gcc atc ttg gca gtg gct gtt ggt
                                                                     107
Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val Gly
                        -10
ttc cca gtc tct caa gac cak gaa cga gaa aaa aga agt atc agt gac
                                                                     155
Phe Pro Val Ser Gln Asp Xaa Glu Arg Glu Lys Arg Ser Ile Ser Asp
                                    10
               5
age gat gaa tta get tea ggg ttt ttt gtg tte eet tae eea tat eea
                                                                      203
Ser Asp Glu Leu Ala Ser Gly Phe Phe Wal Phe Pro Tyr Pro Tyr Pro
                                25
ttt cgc cca ctt cca cca att cca ttt cca aga ttt cca tgg ttt aga
                                                                      251
Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe Arg
       35
                           40
                                                                      299
cgt aat ttt cct att cca ata cct gaa tct gcc cct aca act ccc ctt
Arg Asn Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Thr Thr Pro Leu
                       55
                                                                      351
ccg agc gaa aag taaacaagaa ggaaaagtca cgataaacct ggtcacctga
Pro Ser Glu Lys
65
                                                                      411
aattgaaatt gagccacttc cttgargaat caaaattcct gttaataaaa gaaaaacaaa
tgtaattgaa atagcacaca gcatteteta gteaatatet ttagtgatet tetttaataa
                                                                      471
                                                                      493
acatgaaagc aaaaaaaaa aa
<210> 288
<211> 521
<212> DNA
```

<213> Homo sapiens

<220>

<221> CDS

<222> 96..302

<221> sig_peptide

<222> 96..182

<223> Von Heijne matrix score 5 seg ELSLLPSSLWVLA/TS

<221> polyA_site

<222> 501..514

WO 99/31236 -208- PCT/IB98/02122

<400> 288

aagagacgtc accggctgcg cccttcagta tcgcggacgg aagatggcgt ccgccacccg tctcatccag cggctgcgga actgggcgtc cgggc atg acc tgc agg gga agc Met Thr Cys Arg Gly Ser -25	60 113
tgc agc tac gct acc agg aga tct cca agc gaa ctc agc ctc ctc cca Cys Ser Tyr Ala Thr Arg Arg Ser Pro Ser Glu Leu Ser Leu Leu Pro -20 -15	161
age tee etg tgg gte eta gee aca age tet eea aca att act att gea Ser Ser Leu Trp Val Leu Ala Thr Ser Ser Pro Thr Ile Thr Ile Ala	209
ctc gcg atg gcc gcc ggg aat ctg tgc ccc ctt cca tca tca tkt cgt Leu Ala Met Ala Ala Gly Asn Leu Cys Pro Leu Pro Ser Ser Xaa Arg 10 15 20 25	257
crc aaa agg cgc tgg tgt cag gca asc car caa ara gct ctg ctg Xaa Lys Arg Arg Trp Cys Gln Ala Xaa Gln Gln Xaa Ala Leu Leu 30 35 40	302
tagetgecae tgaaaaraag geggtgaete cageteetee cataaagagg tgggagetgt	362
ceteggaeca geettacetg tgacactgca eceteaegge caccegaeta etttgeetee	422
ttggatttcc tccagggaga atgtgaccta atttatgaca aatacgtara gctcaggtat	482 521
cacttctagt tttactttaa aaaataaaaa aatagagac	344
<210> 289	
<211> 811 <212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 161526	
<221> sig peptide	
<222> 161328	
<223> Von Heijne matrix	
score 4.19999980926514	
seq XSPLLTLALLGQC/SL	
<221> polyA site	
<222> 799811	
<400> 289	60
aaaaaattgc agtgctgaag acactggacc cgcaaaaggc tgtccctccc aaacctggga ttctgggctc actgagttca cctgcgagtc agccctacct gcactgctct ggtctagtac	120
aaacaggctg ctggcattga ggtctgctac aaaaanarta atg gtc cca tgg ccc	175
Met Val Pro Trp Pro	
-55	
agg ggc aag gtg aaa act gct cct att ccc atc tct agg ttt cct ttc	223
Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Ile Ser Arg Phe Pro Phe	
-50 -45 -40 ctc cct acc cac gac cca ccc acc cca gca cat tgg tct cca gca tct	271
Leu Pro Thr His Asp Pro Pro Thr Pro Ala His Trp Ser Pro Ala Ser	
-35 -30 -25 -20	
cat cag cag tit aaa cat kkg toa ooc oto oto act tig goo otg otg	319
His Gln Gln Phe Lys His Xaa Ser Pro Leu Leu Thr Leu Ala Leu Leu	
-15 -10 -5 ggt cag tgc tct ctg ttc arc aat ttg agg aaa aaa ctt gca ggg caa	367
Gly Gln Cys Ser Leu Phe Xaa Asn Leu Arg Lys Lys Leu Ala Gly Gln	
1 S 10	
aaa gca aaa aaa tta cct tcc ttc tcc agc ctg ccc ctg aca ctc tgg	415

15 20 25 CCa tta act cct caa ttt gct gag ctc act aca gtg gca caa aaa aa 4 Pro Leu Thr Pro Gln Phe Ala Glu Leu Thr Thr Val Ala Gln Lys Lys 30 35 40 45	
Pro Leu Thr Pro Gln Phe Ala Glu Leu Thr Thr Val Ala Gln Lys Lys	63
	11
Leu Arg Trp Ser Gly Thr Leu Gly Trp Gly Pro Val Pro Ser Trp Val	
50 55 60	
	66
Gln Phe Phe Leu Gly 65	
15	
	526 586
	746
	306
	311
<210> 290	
<211> 625	
<212> DNA	
<213> Homo sapiens	
.000	
<220>	
<221> CDS <222> 210332	
<221> sig peptide	
<222> 210299	
<223> Von Heijne matrix	
score 8.10000038146973	
seq ITCLLAFWVPASC/IQ	
<221> polyA_signal .	
<222> 594599	
<222> 594599	
<221> polyA_site	
<221> polyA_site <222> 613625	
<221> polyA_site <222> 613625 <400> 290	
<221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg	60
<221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa	120
<221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg	120 180
<221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcetecta etgettetet atcatgtgge cagagetate ttecetaaaa atgcattgea tagttgatca agtcactete tggeetaaaa cetteettgg etecetgetg eceteaggat aaagtetgga ececteage atg get tgt gag act cat ggt gtc	120
<221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcetccta ctgcttctct atcatgtggc cagagetatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc Met Ala Cys Glu Thr His Gly Val	120 180
<pre><221> polyA_site <222> 613.625 <400> 290 acaggtcsmc ttaacatoto ttgatttgag coactoccac tgtcatcago tttcacctgg attatcgtga cagootocta ctgottotot atcatgtgge cagagetato ttccctaaaa atgcattgca tagttgatca agtcactoto tggootaaaa cottcottgg ctccctgctg ccctcaggat aaagtctgga cccctcage atg got tgt gag act cat ggt gtc</pre>	120 180 233
<pre><221> polyA_site <222> 613. 625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180
<pre><221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcage atg gct tgt gag act cat ggt gtc</pre>	120 180 233
<pre><221> polyA_site <222> 613. 625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcage atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281
<pre><221> polyA_site <222> 613. 625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233
<pre><221> polyA_site <222> 613.625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcage atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281
<pre><221> polyA_site <222> 613. 625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcage atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281 329
<pre><221> polyA_site <222> 613.625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcage atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281
<pre><221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcage atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281 329
<pre><221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcage tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtgge cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcage atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281 329 382 442
<pre><221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctggtg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281 329
<pre><221> polyA_site <222> 613625 <400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcage tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtgge cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcage atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281 329 382 442 502

<210> 291

```
<211> 684
  <212> DNA
  <213> Homo sapiens
 <220>
 <221> CDS
 <222> 212..361
 <221> sig_peptide
 <222> 212..319
 <223> Von Heijne matrix
       score 4.09999990463257
       seq HWLFLASLSGIKT/YQ
 <221> polyA_signal
 <222> 650..655
 <221> polyA_site
 <222> 673..684
 <400> 291
atccccawns cactetetea cagagactgt tetttteett etgagaceet actecagett
gtagttctaa atctgtgatt atgcactgtc tgtcttcctc ttgaggtcag gggccatttc
                                                                       120
ttttgttctc tgctatgctc aggacccaga tcaaaggagc tcagtaacta tttacaggcg
                                                                       180
tacatcatat gtggaggaca cttatgctgt g atg gcc cca cac aca gct tcc
                                                                       232
                                    Met Ala Pro His Thr Ala Ser
                                        -35
ttt ggg gtc tgt ccc ctg ctc tcc gtt acc cgc gtg gta gcc act gag
                                                                       280
Phe Gly Val Cys Pro Leu Leu Ser Val Thr Arg Val Val Ala Thr Glu
                                     -20
cac tgg ctc ttc ctg gct tca ctc tct ggc atc aaa act tat cag tcc
                                                                      328
His Trp Leu Phe Leu Ala Ser Leu Ser Gly Ile Lys Thr Tyr Gln Ser
            - 10
                                 -5
                                                     1
tac atc tca gtc ttt tgc aag gtg aca ctt atc tgattaccta attcacacra
                                                                      381
Tyr Ile Ser Val Phe Cys Lys Val Thr Leu Ile
aggtgttaat ggtggtaatg gcataktatt tattacccca ggggacccak aacggtggta
                                                                      441
tcaaaacata tcattcccca gtggtttaaa actctggtag ctttccargg aatccaaagt
                                                                      501
ggaatccagt ctccttagct gawttcacag ggccccgtct gcacaacttg gcttctgtcg
                                                                      561
getteectan ecetgaette ceaageetta gteateacce teteteccae ecagggetea
                                                                      621
gcacagtacc tggaacagtc aagccctcaa taaatgttta ctgagtgcat yaaaaaaaa
                                                                      681
aaa
                                                                      684
<210> 292
<211> 628
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 75..482
<221> sig_peptide
<222> 75..128
<223> Von Heijne matrix
```

score 3.59999990463257 seq KMLISVAMLGAXA/GV

<221> polyA signal <222> 595..600 <221> polyA site <222> 618..627 <400> 292 aagtgagacc gcgcggcaac agcttgcggc tgcggggagc tcccgtgggc gctccgctgg ctgtgcagge ggcc atg gat tcc ttg cgg aaa atg ctg atc tca gtc gca 110 Met Asp Ser Leu Arg Lys Met Leu Ile Ser Val Ala -15 atg ctg ggc gca rgg gct ggc gtg ggc tac gcg ctc ctc gtt atc gtg 158 Met Leu Gly Ala Xaa Ala Gly Val Gly Tyr Ala Leu Leu Val Ile Val 1 acc ccg gga gag cgg cgg aag cag gaa atg cta aag gag atg cca ctg 206 Thr Pro Gly Glu Arg Arg Lys Gln Glu Met Leu Lys Glu Met Pro Leu 15 20 Gln Asp Pro Arg Ser Arg Glu Glu Ala Ala Arg Thr Gln Gln Leu Leu 35 ctg gcc act ctg cag gag gca gcg acc acg cag gag aac gtg gcc tgg 302 Leu Ala Thr Leu Gln Glu Ala Ala Thr Thr Gln Glu Asn Val Ala Trp 50 agg aag aac tgg atg gtt ggc ggc gaa ggc ggc gcc acg gga kgt cac 350 Arg Lys Asn Trp Met Val Gly Gly Glu Gly Gly Ala Thr Gly Xaa His 65 cgt gag acc gga ctt gcc tcc gtg ggc gcc gga cct tgg ctt ggg cgc 398 Arg Glu Thr Gly Leu Ala Ser Val Gly Ala Gly Pro Trp Leu Gly Arg 80 85 agg aat ccg agg cag ctt tct cct tcg tgg gcc can cgg aaa atc cgg 446 Arg Asn Pro Arg Gln Leu Ser Pro Ser Trp Ala Xaa Arg Lys Ile Arg 95 100 amc gaa aat wcc atg cca gga ctc tcc ggg gtc ctg tgaactgccg 492 Xaa Glu Asn Xaa Met Pro Gly Leu Ser Gly Val Leu tegggtgage acgtgteece caaaccetgg actgactget ttaaggteeg caaggeggge 552 cagggccgag acgcgagtcg gatgtggtga actgaaagaa ccaataaaat catgttcctc cammcaaaaa aaaaah

```
<210> 293
```

<220>

<221> CDS

<222> 50..631

<221> sig_peptide

<222> 50..244

<223> Von Heijne matrix score 8 seq LTLIGCLVTGVES/KI

<221> polyA_signal

<222> 777..782

<221> polyA site

<222> 801..812

<211> 813

<212> DNA

<213> Homo sapiens

<400> 293	
aaggaaagga ttactcgagc cttgttagaa tcagacatgg cttcagggg atg cag g Met Gln A -65	
gct ccc ctg agc tgc ctg tca ccg act aag tgg agc agt gtt tct tcc Ala Pro Leu Ser Cys Leu Ser Pro Thr Lys Trp Ser Ser Val Ser Ser -60 -55 -50	106
gca gac tca act gag aag tca gcc tct gcg gca ggc acc agg aat ctg Ala Asp Ser Thr Glu Lys Ser Ala Ser Ala Ala Gly Thr Arg Asn Leu -45 -40 -35	154
cct ttt cag ttc tgt ctc cgg cag gct ttg agg atg aag gct gcg ggc Pro Phe Gln Phe Cys Leu Arg Gln Ala Leu Arg Met Lys Ala Ala Gly -30 -25 -20 -15	202
att ctg acc ctc att ggc tgc ctg gtc aca ggc gtc gag tcc aaa atc Ile Leu Thr Leu Ile Gly Cys Leu Val Thr Gly Val Glu Ser Lys Ile -10 -5	250
tac act cgt tgc aaa ctg gca aaa ata ttc tcg agg gct ggc ctg gac Tyr Thr Arg Cys Lys Leu Ala Lys Ile Phe Ser Arg Ala Gly Leu Asp 5 10 15	298
aat cyg agg ggc ttc agc ctt gga aac tgg atc tgc atg gcg tat tat Asn Xaa Arg Gly Phe Ser Leu Gly Asn Trp Ile Cys Met Ala Tyr Tyr 20 25 30	346
gag agc ggc tac aac acc aca gcc car acg gtc ctg gat gac ggc agc Glu Ser Gly Tyr Asn Thr Thr Ala Gln Thr Val Leu Asp Asp Gly Ser 35	394
atc gac tay ggc atc ttc caa atc aac agc ttc gcg tgg tgc aga cgc Ile Asp Tyr Gly Ile Phe Gln Ile Asn Ser Phe Ala Trp Cys Arg Arg 55 60 65	442
gga aag ctg aag gag aac aac cac tgc cay gtc gcc tgc tca gcc ttg Gly Lys Leu Lys Glu Asn Asn His Cys His Val Ala Cys Ser Ala Leu 70 75 80	
rtc act gat gac ctc aca gat gca att atc tgt gcc arg aaa att gtt Xaa Thr Asp Asp Leu Thr Asp Ala Ile Ile Cys Ala Xaa Lys Ile Val 85 90 95	
aaa gag aca caa gga atg aac tat tgg caa ggc tgg aag aaa cay tgt Lys Glu Thr Gln Gly Met Asn Tyr Trp Gln Gly Trp Lys Lys His Cys 100 105 110	
gag ggg aga gac ctg tcc gas tgg aaa aaa ggc tgt gag gtt tcc Glu Gly Arg Asp Leu Ser Xaa Trp Lys Lys Gly Cys Glu Val Ser 115 120 125	631
taaactggaa ctggacccag gatgctttgc ascaacgccc tagggtttgc agtgaatg caaatgcctg tgtcatcttg tcccgtttcc tcccaatatt ccttctcaaa cttggaga gaaaattaag ctatactttt aagaaaataa atatttccat ttaaatgtca amaaaaaa ah	.gg 751

<210> 294

<211> 778

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 154..576

<221> sig_peptide

<222> 154..360

<223> Von Heijne matrix score 4.80000019073486 seq MMVLSLGIILASA/SF

```
<221> polyA_signal
 <222> 737..742
 <221> polyA site
 <222> 763..775
 <400> 294
agtaaaaaa cactggaata aggaagggct gatgactttc agaagatgaa ggtaagtaga
                                                                       60
 aaccgttgat gggactgaga aaccagagtk aaaacctctt tggagcttct gaggactcag
                                                                      120
ctggaaccaa cgggcacagt tggcaacacc atc atg aca tca caa cct gtt ccc
                                      Met Thr Ser Gln Pro Val Pro
aat gag acc atc ata gtg ctc cca tca aat gtc atc aac ttc tcc caa
                                                                      222
Asn Glu Thr Ile Ile Val Leu Pro Ser Asn Val Ile Asn Phe Ser Gln
                             -55
gca gag aaa ccc gaa ccc acc aac cag ggg cag gat agc ctg aag aaa
                                                                      270
Ala Glu Lys Pro Glu Pro Thr Asn Gln Gly Gln Asp Ser Leu Lys Lys
                         -40
                                             - 35
cat cta cac gca gaa atc aaa gtt att ggg act atc cag atc ttg tgt
                                                                      318
His Leu His Ala Glu Ile Lys Val Ile Gly Thr Ile Gln Ile Leu Cys
                    -25
                                         -20
ggc atg atg gta ttg agc ttg ggg atc att ttg gca tct gct tcc ttc
                                                                      366
Gly Met Met Val Leu Ser Leu Gly Ile Ile Leu Ala Ser Ala Ser Phe
                -10
                                     - 5
tot coa aat tit acc caa gtg act tot aca ctg ttg aac tot got tac
                                                                      414
Ser Pro Asn Phe Thr Gln Val Thr Ser Thr Leu Leu Asn Ser Ala Tyr
                            10
cca ttc ata gga ccc ttt ttt gtr akt aaa btt tct gag gag ggc agg
Pro Phe Ile Gly Pro Phe Phe Val Xaa Lys Xaa Ser Glu Glu Gly Arg
                        25
                                             30
atg ggg caa ara ggg gag gaa rat vcc aat agc tta aac ttc cca sct
                                                                      510
Met Gly Gln Xaa Gly Glu Glu Xaa Xaa Asn Ser Leu Asn Phe Pro Xaa
35
                    40
                                        45
gcc agc ttg cta tkt ttg atc tgc cag gav caa gga ttc aac ggt gaa
                                                                      558
Ala Ser Leu Leu Xaa Leu Ile Cys Gln Xaa Gln Gly Phe Asn Gly Glu
                55
                                                        65
tot tgt tot cot gtc ggg targataaca ggggttgott rattttagat
                                                                      606
Ser Cys Ser Pro Val Gly
caatttetta teagaeteaa ataaaeattt ettttgaaaa teatettatt etteaeatta
                                                                      666
tcatcttgag ctatgatgga aactagtgas ktctctccag gtttaggcga aaaaaaaatc
                                                                      726
catgaattag gataaagttg ggaaggaaca ttttatacaa aaaaaaaaah cc
                                                                      778
```

<210> 295

<211> 1060

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 154..897

<221> sig_peptide

<222> 154..360

<223> Von Heijne matrix score 4.80000019073486 seq MMVLSLGIILASA/SF

<221> polyA_signal

<222> 1017..1022

<221> polyA_site <222> 1044..1054

. 4.0	• •															
	0 > 29 aaaaa		cacto	ggaal	ca ac	gaac	raact	: gat	gact	ttc	agaa	gato	aa c	gtaa	gtaga	60
															ctcag	120
															ccc	174
									Met	Thr	Ser	Gln	Pro	Val	Pro	
													-65			
						ctc										222
Asn	GIU	-60	11e	ile	vai	Leu		Ser	Asn	Val	He		Phe	Ser	Gln	
aca.	aaa		ccc	m = =	ccc	acc	-55	C 2 C		c 3 G	aa+	-50	cto	330	333	270
						Thr										270
	-45	-,-				-40		41	U 1 <i>y</i>	01	-35	501		2,0	2,3	
cat	cta	cac	gca	qar	rtc	aaa	gtt	att	qqq	act		caq	atc	ttq	tqt	318
			_	_		Lys	_					-		_	_	
-30					-25					-20					-15	
	_	-	_	-	_	ttg				_	_		_			366
Gly	Met	Met	Val		Ser	Leu	Gly	Ile		Leu	Ala	Ser	Ala	Ser	Phe	
				-10					- 5					1		
						gtg										414
ser	Pro	Asn 5	Pne	inr	GIN	Val	10	ser	Thr	reu	Leu	Asn 15	ser	Ala	Tyr	
cca	ttc	_	aa.	ccc	+++	ttt		atc	atc	tct	aac		cta	tca	atc	462
						Phe										
	20		1			25					30					
gcc	aca	aaa	aaa	agg	tta	acc	aac	ctt	ttg	gtg	cat	acc	acc	ctg	gtt	510
Ala	Thr	Lys	Lys	Arg	Leu	Thr	Asn	Leu	Leu	Val	His	Thr	Thr	Leu	Val	
35				_	40					45					50	
	_		_	_	_	ctg		_	_					-	_	558
Gly	Ser	Ile	Leu	Ser	Ala	Leu	Ser	Ala	Leu	Val	Gly	Phe	Ile		Leu	
				55					60					65		
	_		_	-		tta			_		_		_		_	606
ser	vai	Lys	70	Ата	Inr	Leu	Asn	75	АТА	ser	rea	хаа	80	Gru	Leu	•
ame	222	22 +		a + a	CC2	aca	272		+=+	a++	vc+	tac		tat	cat	654
						Thr										•••
****	-,,-	85					90		-1-			95		-1-		
gat	tca	ctt	tat	acc	acg	gac	kgc	tat	aca	gcc	aaa	gcc	akt	ctg	gct	702
						Asp										
	100					105				-	110					
						ctg										750
-	Thr	Leu	Ser	Leu		Leu	Ile	Cys	Thr		Leu	Glu	Phe	Cys		
115					120					125					130	200
sct	gtg	ctc	act	gct	gtg	ctg	cgg	tgg	aaa	cag	gct	tac	tct	gac	ttc	798
хаа	vai	Leu	Thr			Leu	Arg	Trp		GIn	Ala	Tyr	Ser	145		
	~~~	<del>-</del>	~+ ·	135		a <b>-</b> a	ca+	C 3 T	140	F 3.0	a + +	aau	225		ggm	846
															Gly	010
PIO	GIY	261	150	Deu	FIIC	Deu	110	155	361	1 7 1	116	GI	160		017	
ato	tcc	tca		ato	acv	cat	gac		gga	tat	gaa	gaa			act	894
															Thr	
		165	-1-				170		1			175			•	
tct	taa		aaa (	ggga	gaaa	ta t			a ag	ttga	ttct			ata		947
Ser		-			_			-	_	-						
															tttaaa	1007
gta	atga	aca	ttaa	aaaa	aa c	catt	attt	c ac	tgtc	aaaa	aaa	aaaa	mcc	nkt		1060

```
<210> 296
<211> 444
<212> DNA
<213 > Homo sapiens
<220>
<221> CDS
<222> 146..292
<221> sig_peptide
<222> 146..253
<223> Von Heijne matrix
      score 5.5
      seq FTSMCILFHCLLS/FQ
                               45.0
<221> polyA_signal
<222> 395..400
<221> polyA_site
<222> 433..444
<400> 296
aacttgggac aagaratcaa actttaaaga tggtctaaag cccctcttaa aggtctgact
                                                                  60
gtgtcggacc tctagagcta atctcactag atgtgagcca ttgtttatat tctagccatc
                                                                 120
ctttcatttc attctagaag acccc atg caa gtt ccc cac cta agg gtc tgg
                                                                 172
                          Met Gln Val Pro His Leu Arg Val Trp
                              -35
                                                 -30
aca cag gtg awa gat acc ttc att ggt tat aga aat ttg gga ttt aca
                                                                 220
Thr Gln Val Xaa Asp Thr Phe Ile Gly Tyr Arg Asn Leu Gly Phe Thr
       -25
                          -20
                                             -15
agt atg tgc ata ttg ttc cac tgt ctt ctt agc ttt cag gtt ttc aaa
                                                                  268
Ser Met Cys Ile Leu Phe His Cys Leu Leu Ser Phe Gln Val Phe Lys
    -10
                     -5
                                         1
aag aaa aga aaa ctt ara ctt ttc tgatgttctt ttttacgtaa ataaccattt
                                                                  322
Lys Lys Arg Lys Leu Xaa Leu Phe
               10
tattgttgtt ttgctttttc tgccttcaaa ctactcccac aggccaaata tavctggctg
442
                                                                  444
<210> 297
<211> 754
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 126..383
<221> sig_peptide
<222> 126..167
<223> Von Heijne matrix
      score 7.5
      seg VALNLILVPCCAA/WC
<221> polyA_signal
<222> 726..731
```

<221> polyA_site <222> 743..754

<400> 297 aattgtatgt tacgatgttg tattgatttt taagaaagta attkratttg taaaacttct	60
gctcgtttac actgcacatt gaatacaggt aactaattgg wwggagaggg gaggtcactc	120
ttttg atg gtg gcc ctg aac ctc att ctg gtt ccc tgc tgc gct gct tgg	170
Met Val Ala Leu Asn Leu Ile Leu Val Pro Cys Cys Ala Ala Trp	
-10 -5 1 tgt gac cca cgg agg atc cac tcc cag gat gac gtg ctc cgt agc tct	218
Cys Asp Pro Arg Arg Ile His Ser Gln Asp Asp Val Leu Arg Ser Ser	210
5 10 15	
gct gct gat act ggg tct gcg atg cag cgg cgt gag gcc tgg gct ggt	266
Ala Ala Asp Thr Gly Ser Ala Met Gln Arg Arg Glu Ala Trp Ala Gly	
20 25 30 tog aga agg toa caa coo the bet gtt ggt etg eet tet get gaa aga	314
Trp Arg Arg Ser Gln Pro Phe Ser Val Gly Leu Pro Ser Ala Glu Arg	31.
35 40 45	
ctc gag aac caa cca ggg aag ctg tcc tgg agg tcc ctg gtc gga gag	362
Leu Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg Ser Leu Val Gly Glu	
50 55 60 65 gga cat aga atc tgt gac ctc tgacrrctgt gaasccaccc tgggctacar	413
Gly His Arg Ile Cys Asp Leu	
70	
aaaccacagt cttcccagca attattacaa ttcttgaatt ccttggggat tttttactgc	473
cctttcaaag cacttaaktg tkrratctaa cgtkttccag tgtctgtctg aggtgactta	533 593
aaaaatcaga acaaaacttc tattatccag agtcatggga gagtacaccc tttccaggaa taatgttttg ggaaacactg aaatgaaatc ttcccagtat tataaattgt gtatttaaaa	653
aaaagaaact tttctgaatg cctacctggc ggtgtatacc aggcagtgtg ccagtttaaa	713
aagatgaaaa agaataaaaa cttttgagga aaaaaaaaaa	754
•	
<210> 298	
<211> 629	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 66497	
<221> sig_peptide	
<222> 66239	
<pre>&lt;223&gt; Von Heijne matrix score 5.40000009536743</pre>	
seq QLLDSVLWLGALG/LT	
<221> polyA_signal	
<222> 594599	
<221> polyA_site	
<222> 618629	
<400> 298	60
aactcccaga atgctgacca aagtgggagg agcactaggt cttcccgtca cctccacctc tctcc atg acc cgg ctc tgc tta ccc aga ccc gaa gca cgt gag gat ccg	110
Met Thr Arg Leu Cys Leu Pro Arg Pro Glu Ala Arg Glu Asp Pro	
-55 -50 -45	
ato oca gtt cot oca agg ggo otg ggt got ggg gag ggg toa ggt agt	158
Ile Pro Val Pro Pro Arg Gly Leu Gly Ala Gly Glu Gly Ser Gly Ser	
-40 -35 -30 cca gtg cgt cca cct gta tcc acc tgg ggc cct agc tgg gcc cag ctc	206
Pro Val Arg Pro Pro Val Ser Thr Trp Gly Pro Ser Trp Ala Gln Leu	200
120 122 129 120 120 121 122 122 125 127 127 127 127 127 127 127 127 127 127	

-25 -20 -15	
ctg gac agt gtc cta tgg ctg ggg gca cta gga ctg aca atc cag gca Leu Asp Ser Val Leu Trp Leu Gly Ala Leu Gly Leu Thr Ile Gln Ala	254
-10 -5 1 5	
gto tit too ace act ggo coa goo otg otg otg ott otg gto ago tto	302
Val Phe Ser Thr Thr Gly Pro Ala Leu Leu Leu Leu Leu Val Ser Phe	
10 15 20	
ctc acc ttt gac ctg ctc cat agg ccc gca gtc aca ctc tgc cac agc	350
Leu Thr Phe Asp Leu Leu His Arg Pro Ala Val Thr Leu Cys His Ser	
25 30 35	
gca aac ttc tca cca ggg gcc aga gtc agg ggg ccg gtg aag gtc ctg	398
Ala Asn Phe Ser Pro Gly Ala Arg Val Arg Gly Pro Val Lys Val Leu 40 45 50	
40 45 50 gac agc agg agg ctc tac tcc tgc aaa tgg gta cag tct cag gac aac	116
Asp Ser Arg Arg Leu Tyr Ser Cys Lys Trp Val Gln Ser Gln Asp Asn	446
55 60 65	
tta gee tee agg aag cae tge tge tge tea tgg gge tgg gee ege	494
Leu Ala Ser Arg Lys His Cys Cys Cys Ser Trp Gly Trp Ala Arg	
70 75 80 85	
toc tgaaaacctg tggcatgccc ttgwaccctg cttggcctgg ctttctgcct	547
Ser	
ccatcettgg geetgakane eceteceeae aacteagtgt eetteaaata tacaatgace	607
accettette aaaaaaaaa aa	629
<210> 299	
<210> 299 <211> 765	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 49411	
<221> sig_peptide	
<222> 4996	
<223> Von Heijne matrix	
score 10.100003814697	
seq LVLTLCTLPLAVA/SA	
<221> polyA signal	
<222> 732737	
<221> polyA_site	
<222> 750763	
<400> 299	
aaagatooot goagoooggo aggagagaag gotgagoott otggogto atg gag agg	57
Met Glu Arg	
-15	
ctc gtc cta acc ctg tgc acc ctc ccg ctg gct gtg gcg tct gct ggc	105
Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala Ser Ala Gly	
-10 -5 1	
tgc gcc acg acg cca gct cgc aac ctg agc tgc tac cag tgc ttc aag	153
Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln Cys Phe Lys	

gtc agc agc tgg acg gag tgc ccg ccc acc tgg tgc agc ccg ctg gac Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser Pro Leu Asp 20 25 30 35 caa gtc tgc atc tcc aac gag gtg gtc gtc tct ttt agt gag tcy ccc Gln Val Cys Ile Ser Asn Glu Val Val Val Ser Phe Ser Glu Ser Pro

201

40

45

50

			4.5	50	
ccg ggc ag Pro Gly Ar	a ggg cas gtg g Gly Xaa Val 55	cca bgt gcc Pro Xaa Ala 60	ggg gaa k Gly Glu X	gg ccg gtg cc aa Pro Val Pro	c ccg 297 o Pro
cct ctc wk Pro Leu Xa 70	c gac tta bct a Asp Leu Xaa	atg act cct Met Thr Pro	cgg ckc y Arg Xaa X	cc agg gcc tg aa Arg Ala Tr 80	g ggc 345 p Gly
cck gtg gg Pro Val Gl: 85	t ccd aaa gtg y Pro Lys Val	cct cct gct Pro Pro Ala 90	gtc tct c Val Ser P	cc gcg ctg gg ro Ala Leu Gl	c tcg 393 y Ser
ggc gag car Gly Glu His 100	ccs rva btg Pro Xaa Xaa 105				441
agtgtcacta	ggaactqtca q	caggacaaa gg	ctctgatg to	cactgaatt tac	aaaraca 501
gcaggaacrs	ackggtgggg a	tgggcagct gt	tcrarger a	tgggtkatc tgc	ccttcct 561
ggcacagcac	artacacctg c	catacaacc ca	rcatcage c	akgctgcac tgg	aatcqat 621
acagtgtatg	acaatgtcat a	tagtataac ac	aacataat g	aatataacg tgt	atattqc 681
aacttaatat	aatacgatgt a	atataatgo ta	cataatac a	acataatat aata	anaatag 741
	aaaaaaaaa a				765
<pre></pre>	eptide 6 leijne matrix 10.1000038 VLTLCTLPLAVA _signal 598	14697			
<400> 300 aaagatccct	gcagcccggc a	ggagagaag gc	tgagcett c		ag agg 57 lu Arg .
ctc gtc cta	acc ctg tgc	acc ctc ccq	ctq act a	tg gcg tct gc	
Leu Val Leu	Thr Leu Cys	Thr Leu Pro	Leu Ala V	al Ala Ser Al 1	a Gly
tgc gcc acc	acg cca gct	cgc aac ctg	agc tgc t	ac cag tgc tt	c aag 153
	Thr Pro Ala		Ser Cys T	yr Gln Cys Ph	e Lys
5		10	1		
				gc agc ccg ct	
				ys Ser Pro Le	
20	25	-	30	-	35
caa gtc toc		gag gtg gtc		tt aaa tgg ag	
				he Lys Trp Se	
	40		45	50	
cac atc ctr		cac tat act		gt ccc aac ga	
				ys Pro Asn As	
y var bet	55	60	FIO Aty C	ys Pro Asii As 65	h wan
	J.J	60		00	•

WO 99/31236 -219- PCT/IB98/02122

								ccc Pro			Gln					345
		tgc						tgc Cys								393
								GJÀ aaa								441
								cca Pro								489
								cca Pro 140								534
			gccc					999	gacca	icra	ctto	acco	tc t	tg <b>g</b> a	aracaa	594 623
<210	·> 30	)1			•											
	> 57	_														
	> DN															
<213	> HC	omo s	apie	ens												
<220	>				•											
	> CI	-														
<222	> 86	541	L <b>5</b>		•											
<221	.> si	g pe	ptic	le												
<222	> 86	14	15		•											
<223			eijne													
			9.80				5									
	se	q r	rigli	اطاطاطا	3XQA/	MP										
<221	.> pc	olyA_	sign	nal												
<222	> 54	105	45													
-221	> nc	1112	site													•
	2> 56			•												
	> 3(	_												cc	22442	60
adaa	iacto Igaaa	ac d	cagi	gagı saaa:	eg co	gago	atto	a ay	cta	atoc	gta	ctt	aya att	ttc	aaggaa acc	112
-5	-9				-, -,		Met	Xaa	Leu	Met	Val	Leu	Val	Phe	Thr	
							-20					-15				
att	ggg	cta	act	ttg	ctg	cta	gga	rtt	caa	gcc	atg	cct	gca	aat	cgc	160
Ile	-10	Leu	Thr	Leu	Leu	Leu -5	GIY	хаа	GIn	Ala	Met 1	Pro	Ala	ASI	Arg 5	
ctc		tac	tac	aga	aag	_	cta	aaa	qat	cac	_	tgt	cac	aac	ctt	208
Leu	Ser	Cys	Tyr	Arg	Lys	Ile	Leu	Lys	Āsp	His	Asn	Cys	His	Asn	Leu	
				10					15					20		0.5
ccg	gaa	gga	gta	gct	gac	ctg	aca	cag	att	gat	gto	aat	gto	cag	gat	250
Pro	GIU	GTA	Va 1 25	ATA	Asp	ьeu	rnr	30	тте	ASP	val	ASN	. vai	. GII	Asp	
cat	ttc	tga		gqa	aaq	gga	tgt		atg	ato	tgt	tac		aac	ttc	30
His	Phe	Trp	Asp	Gly	Lys	Gly	Cys	Glu	Met	Ile	. Cys	Tyr	Cys	Ası	n Phe	
		40					45					50				35
aag	cga	att	gct	ctg	ctg	CCC	aaa	aga	cgt Arc	. ttt . ph=	Ctt	. cgg	aco Thi	. aaa	a gat s Asp	35
nys	SS	116	wid	nen	חבת	60	- Lys	, Arg	, Arg	1 5.116	65		* * *	,		
														v +=1	rrct	4.0

Leu Phe Arg Asp Ser Leu Gln Gln Ser Met Arg Ile Phe Met Tyr Ser 70 75 80 85	
ggc gaa cac cat tcc tgatttccca caaactgcac tacatcagta taactgcatt Gly Glu His His Ser 90	455
tctagtttct atatagtgca atagagcata gattctataa attcttactt gtctaagaaa gtaaatctgt gttaaacaag tagtaataaa agttaattca atccaaaaaa aaaaaa	515 571
<210> 302 <211> 612 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 56268	
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 56100 &lt;223&gt; Von Heijne matrix</pre>	
<221> polyA_signal	
<221> polyA_site <222> 601612	
<400> 302 ctaatcgaaa agggggattt teeggtteeg geetggegag agtttgtgeg gegae atg Met -15	58
aaa ctg ctt acc cac aat ctg ctg agc tcg cat gtg cgg ggg gtg ggg Lys Leu Leu Thr His Asn Leu Leu Ser Ser His Val Arg Gly Val Gly -10 -5	106
tcc cgt ggc ttc ccc ctg cgc ctc cag gcc acc gag gtc cgt atc tgc Ser Arg Gly Phe Pro Leu Arg Leu Gln Ala Thr Glu Val Arg Ile Cys 5	154
cct gtg gaa ttc aac ccc aac ttc gtg gcg cgt atg ata cct aaa gtg Pro Val Glu Phe Asn Pro Asn Phe Val Ala Arg Met Ile Pro Lys Val 20 25 30	202
gag tgg tcg gcg ttc ctg gag gcg rmc gat aac ttg cgt ctg atc cag Glu Trp Ser Ala Phe Leu Glu Ala Xaa Asp Asn Leu Arg Leu Ile Gln 35 40 45 50	250
gtg ccg aga agg gcc ggt tgagggatat gaggagaatg aggagtttct Val Pro Arg Arg Ala Gly 55	298
gaggaccatg caccacctgc tgctggaggt ggamstgaka gagggcaccc tgcagtgccc	358
ggaatetgga egtatgttee ceateageeg egggateeee aacatgetge tgagtgaaga	418
ggaaactgag agttgattgt gccaggcgcc agtttttctt gttatgactg tgtatttttg	478
ttgatctata ccctgtttcc gaattctgcc gtgtgtatcc ccaacccttg acccaatgac	538
accaaacaca gtgtttttga gctcggtatt atatattttt ttctcattaa aggtttaaaa	598 612
ccaaaaaaaa aaaa	012

<210> 303 <211> 539

<212> DNA

```
<213> Homo sapiens
<220>
<221> CDS
<222> 32..328
<221> sig_peptide
<222> 32..103
<223> Von Heijne matrix
      score 4.59999990463257
      seq FFIFCSLNTLLLG/GV
<221> polyA signal
<222> 508..513
<221> polyA_site
<222> 528..539
<400> 303
aacaactate etgeetgetg ettgetgeac e atg aag tet gee aag etg gga
                                                                      52
                                   Met Lys Ser Ala Lys Leu Gly
                                                   -20
ttt ctt cta aga ttc ttc atc ttc tgc tca ttg aat acc ctg tta ttg
                                                                     100
Phe Leu Leu Arg Phe Phe Ile Phe Cys Ser Leu Asn Thr Leu Leu Leu
      -15
                            -10
ggt ggt gtt aat aaa att geg gag aag ata tgt gga gac ete aaa gat
Gly Gly Val Asn Lys Ile Ala Glu Lys Ile Cys Gly Asp Leu Lys Asp
                                        10
ccc tgc aaa ttg gac atg aat ttt gga agc tgc tat gaa gtt cac ttt
                                                                     196
Pro Cys Lys Leu Asp Met Asn Phe Gly Ser Cys Tyr Glu Val His Phe
                20
aga tat ttc tac aac aga acc tcc aaa aga tgt gaa act ttt gtc ttc
                                                                     244
Arg Tyr Phe Tyr Asn Arg Thr Ser Lys Arg Cys Glu Thr Phe Val Phe
            35
                                40
tcc agc tgt aat ggc aac ctt aac aac ttc aag ctt aaa ata gaa cgt
                                                                     292
Ser Ser Cys Asn Gly Asn Leu Asn Asn Phe Lys Leu Lys Ile Glu Arq
       50
                            55
gaa gta kcc tgt gtt gca aaa tac aaa cca ccg agg tgagaggatg
                                                                     338
Glu Val Xaa Cys Val Ala Lys Tyr Lys Pro Pro Arg
tgaactcatg aagttgtctg ctgcaccatc cgaaataaag acacaagaaa attcaractg
atttwgaaat ctttgttwta tttccmymak ggcgwktaag cttccatatg tttgctattt
tcctgaccct agttttgtct ttcctggaaa ttaactgtat gakcattasa atgaaagagt
ctttctgtca aaaaaaaaa a
                                                                     539
<210> 304
<211> 964
<212> DNA
<213> Homo sapiens
<220>
```

<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 21..527

<221> sig_peptide
<222> 21..95
<223> Von Heijne matrix
score 8.5
seq_LKVLLLPLAPAAA/QD

<221> polyA_signal <222> 921..926 <221> polyA site <222> 953..963 <400> 304 agggcggate tteteeggee atg agg aag eea gee get gge tte ett eee tea Met Arg Lys Pro Ala Ala Gly Phe Leu Pro Ser -25 -20 ctc ctg aag gtg ctg ctc ctg cct ctg gca cct gcc gca gcc cag gat 101 Leu Leu Lys Val Leu Leu Pro Leu Ala Pro Ala Ala Ala Gln Asp -10 - 5 teg act cag gee tee act eea gge age eet ete tet eet ace gaa tae 149 Ser Thr Gln Ala Ser Thr Pro Gly Ser Pro Leu Ser Pro Thr Glu Tyr 10 caa ego tto tte gea etg etg act eea ace tgg aag gea gar act ace 197 Gln Arg Phe Phe Ala Leu Leu Thr Pro Thr Trp Lys Ala Glu Thr Thr 25 30 tgc cgt ctc cgt gca acc cac ggc tgc cgg aat ccc aca ctc gtc cag 245 Cys Arg Leu Arg Ala Thr His Gly Cys Arg Asn Pro Thr Leu Val Gln 40 45 ctg gac caa tat gaa aac cac ggc tta gtg ccc gat ggt gct gtc tgc 293 Leu Asp Gln Tyr Glu Asn His Gly Leu Val Pro Asp Gly Ala Val Cys 55 60 tee aac etc eet tat gee tee tgg ttt gag tet tte tge eag tte act Ser Asn Leu Pro Tyr Ala Ser Trp Phe Glu Ser Phe Cys Gln Phe Thr 75 cac tac cgt tgc tcc aac cac gtc tac tat gcc aag aga gtc ctg tgt 389 His Tyr Arg Cys Ser Asn His Val Tyr Tyr Ala Lys Arg Val Leu Cys 85 90 95 tee cag cea gte tet att etc tew eet aac act etc aag gag ata gaa 437 Ser Gln Pro Val Ser Ile Leu Ser Pro Asn Thr Leu Lys Glu Ile Glu 105 110 set tea get gaa gte tea eee ace aca gat gae ete eee eat ete ace 485 Xaa Ser Ala Glu Val Ser Pro Thr Thr Asp Asp Leu Pro His Leu Thr 120 125 130 cca ctt cac agt gac aga acg cca gac ctt cca gcc ctg gcc 527 Pro Leu His Ser Asp Arg Thr Pro Asp Leu Pro Ala Leu Ala 140 tgagaggete agcaacaacg tggaagaget cetacaatec teettgteee tgggaggeea ggagcaagcg ccagagcaca agcaggagca aggagtggag cacaggcagg agccgacaca agaacacaag caggaagagg ggcagaaaca ggaagagcaa gaagaggaac aggaagagga 707 gggaaagcag gaagaaggac aggggactaa ggagggacgg gaggctgtgt ctcagctgca 767 gacagactca gageceaagt tteactetga atetetatet tetaaceett cetettttge **B27** tccccgggta cganaagtag agtctactcc tatgataatg gagaacatcc aggagctcat 887 tcgatcagcc caggaaatag atgaaatgaa tgaaatatat gatgagaact cctactggag 947 aaaccaaaaa aaaaaak 964

<210> 305

<211> 684

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 147..647

<221> sig_peptide

<222> 147..374

<223> Von Heijne matrix score 3.5 seq LASASELPLGSRP/AP

<221> polyA_site <222> 668..681

<400> 305	
aacttcctgt gagcccggcg gtgacaacgg caacatggcc cgtgaacgga gctgaagtcg	60
acgacttete etrgrarmee eegactgagg eggagaegaa ggtgetgeag gegegaeggg	120
ageggeaaga tegeatetee eggete atg gge gae tat etg etg ege ggt tae	173
Met Gly Asp Tyr Leu Leu Arg Gly Tyr	
-75 -70	
cgc atg ctg ggc gag acg tgt gcg gac tgc ggg acg atc ctc ctc caa	221
Arg Met Leu Gly Glu Thr Cys Ala Asp Cys Gly Thr Ile Leu Leu Gln	
-65 -60 -55	
gac aaa cag cgg aaa atc tac tgc gtg gct tgt cag gaa ctc gac tca	269
Asp Lys Gln Arg Lys Ile Tyr Cys Val Ala Cys Gln Glu Leu Asp Ser	
-50 -45 -40	
gac gtg gat aaa gat aat ccc gct ctg aat gcc cag gct gcc ctc tcc	317
Asp Val Asp Lys Asp Asn Pro Ala Leu Asn Ala Gln Ala Ala Leu Ser	
-35 -30 -25 -20	
caa got ogg gag cac cag otg god toa god toa gag otc occ otg ggo	365
Gln Ala Arg Glu His Gln Leu Ala Ser Ala Ser Glu Leu Pro Leu Gly	
-15 -10 -5	
tot oga oot gog ood daa ood ooa gta oot ogt oog gag dad tgt gag	413
Ser Arg Pro Ala Pro Gln Pro Pro Val Pro Arg Pro Glu His Cys Glu	
1 5 10	
gga gct gca gga ctc aag gca gcc cag ggg cca cct gct cct gct	461
Gly Ala Ala Ala Gly Leu Lys Ala Ala Gln Gly Pro Pro Ala Pro Ala	
15 20 25	
gtg cet cea aat aca rat gte atg gee tge aca cag aca gee etc ttg	509
Val Pro Pro Asn Thr Xaa Val Met Ala Cys Thr Gln Thr Ala Leu Leu	
30 35 40 45	
caa aag ctg ace tgg gcc tct gct gaa ctg ggc tct anc acc tcc cyg	557
Gln Lys Leu Thr Trp Ala Ser Ala Glu Leu Gly Ser Xaa Thr Ser Xaa	
50 55 60	505
gga aaa mta gca tcc agc tgt gtg gcc tta tcc gcg cat gtg cgg agg	605
Gly Lys Xaa Ala Ser Ser Cys Val Ala Leu Ser Ala His Val Arg Arg	
65 70 75	647
ccc tgc gca gcc tgc agc agc tac agc act aag aga agc ccc	647
Pro Cys Ala Ala Cys Ser Ser Tyr Ser Thr Lys Arg Ser Pro	
80 85 90	C04
tgagaaaac ctctagaaaa acaaaaaaaa aaaaccc	684

<210> 306

<211> 693 <212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 262..471

<221> sig_peptide

<222> 262..306

<223> Von Heijne matrix score 3.5 seq LCFLLPHHRLQEA/RQ

	> polyA_signal > 663668	
	> polyA_site > 682693	
	> 306	
att	gegge getegebgma cyhsgwtgtt cageaeette ggteeggttg aggttgteaa	60
gtc	mccaa acaggitgit tetetgeagi ticcaacatg geagggmsgi tiaatagaca	120
tgga	taagaa gtccactcac agaaatcctg aagatgccag ggctggcaaa tatgaaggta	180
aaca		240
cagt	gacgte tittictica g atg ate eta tgt tie ett ett eet eat eat	291
	. Met Ile Leu Cys Phe Leu Leu Pro His His -15 -10	
cgt		339
Arg	Leu Gln Glu Ala Arg Gln Ile Gln Val Leu Lys Met Leu Pro Arg	
- 5	1 5 10	
gaa	aaa tta aga aga aga gaa gag aga aaa caa ata aat ggg saa aaa	387
	Lys Leu Arg Arg Arg Glu Glu Arg Lys Gln Ile Asn Gly Lys Lys	
	15 20 25	
raa	agg aca aaa tat gaa aca cca aga aaa rga raa gga aaa aaa gga	435
	arg Thr Lys Tyr Glu Thr Pro Arg Lys Xaa Xaa Gly Lys Lys Gly	
	30 35 40	
~~~	· · · · · · · · · · · · · · · · · · ·	
	ac mac cmc wtw tkt cmc ctt tcc aar agg gac tgaaactggg	481
GIÀ	Asn Xaa Xaa Xaa Xaa Leu Ser Lys Arg Asp	
	5 50 55	
	cottt tgatttccaa votcasogtt ttggtgtaag goggocaaar aaggatgogg	541
	agcac tgtgaagcct acaaaaacat tgatgcgctg gcttggggat ttgaatttga	601
	tttca cactaagttc agactcatga aaccaatctt cagatgctct gtaaaccaca	661
taat	laagag tttggaaatt aaaaaaaaar aa	693
<211 <212	307 1656 DNA Homo sapiens	
<220	•	
<221	CDS	
<222	741216	
<221	sig_peptide -	
	74172	
	• Von Heijne matrix	
1227	score 5.80000019073486	
	seq XLCLGMALCPRQA/TR	
	polyA_signal	
<222	16271632	
<221		
	· polyA site	
	> polyA_site > 16401652	
	> polyA_site > 16401652	
-400	16401652	
	307	£ (
atct	• 16401652 • 307 • sttgge gteteaacgt teggateage agetttttte cattetetet etceaettet	60
atct	• 16401652 • 307 • sttgge gteteaaegt teggateage agetttttte eattetetet etecaettet • gagea gee atg agt tgg act gtg eet gtg egg gee age eag	60 109
atct	• 16401652 • 307 • Stigge gteteaaegt teggateage agettitte cattetetet etecaettet • Egagea gee atg agt tgg act gtg egt gtg egg gee age eag — Met Ser Trp Thr Val Pro Val Val Arg Ala Ser Gln	
atct tcag	• 16401652 • 307 • sttggc gtctcaacgt tcggatcagc agcttttttc cattctctct ctccacttct • gagca gcc atg agt tgg act gtg cct gtt gtg cgg gcc agc cag Met Ser Trp Thr Val Pro Val Val Arg Ala Ser Gln -30 -25	109
atct tcag	• 16401652 • 307 • sttggc gtctcaacgt tcggatcagc agcttttttc cattctctct ctccacttct • gagca gcc atg agt tgg act gtg cct gtt gtg cgg gcc agc cag Met Ser Trp Thr Val Pro Val Val Arg Ala Ser Gln -30 -25 • gtg agc tcg gtg gga gcg aat ktc cta tgc ctg ggg atg gcc ctg	
atct tcag	• 16401652 • 307 • sttggc gtctcaacgt tcggatcagc agcttttttc cattctctct ctccacttct • gagca gcc atg agt tgg act gtg cct gtt gtg cgg gcc agc cag Met Ser Trp Thr Val Pro Val Val Arg Ala Ser Gln -30 -25	109

WO 99/31236 -225- PCT/IB98/02122

tgt	ccg	cgt	caa	gca	acg	cgc	atc	ccg	ctc	aac	ggc	acc	tgg	ctc	ttc	205
Cys -5	Pro	Arg	Gln	Ala	Thr 1	Arg	Ile	Pro	Leu 5	Asn	Gly	Thr	Trp	Leu 10	Phe	
acc	ccc	qtq	agc	aaq	atq	aca	act	gtg	aar	agt	pap	ctt	att	gag	cgt	253
Thr	Pro	Val	Ser	Lvs	Met	Ala	Thr	Val	Lys	Ser	Glu	Leu	Ile	Glu	Arg	
			15	-,,				20					25		-	
ttc	act	tcc		аал	ccc	att	cat	cac	agt	aaq	atc	tcc		ata	gga	301
								His								
1110	1111	30	314	цуз	-10	Val	35			<i>-,</i> 3	141	40	110		1	
	~~~			~~~		~~~		~~+	350	200			++=	222	aac	349
acc mb-	gya	cog	grg	990	atg	31-	cgc	gct	Tio	Com	Tla	Lua	LLA	Tuc	230	349
Inr		ser	vaı	GIY	Met		Cys	Ala	116	Ser		Leu	neu	пåэ	Gry	
	45					50					55					205
								gat								397
Leu	Ser	Asp	Glu	Leu		Leu	Val	Asp	Leu		GIU	xaa	rÀa	Leu		
60					65					70					75	
ggt	gag	acr	atg	gat	ctt	caa	cat	ggc	agc	cct	ttc	acg	aaa	atg	cca	445
Gly	Glu	Thr	Met	Asp	Leu	Gln	His	Gly	Ser	Pro	Phe	Thr	Lys		Pro	
				80					85					90		
aat	att	gtt	tgt	agc	aaa	rat	tac	ttt	gtc	aca	gca	aac	tcc	aac	cta	493
Asn	Ile	Val	Cys	Ser	Lys	Xaa	Tyr	Phe	Val	Thr	Ala	Asn	Ser	Asn	Leu	
			95		-		-	100					105			
ata	att	atc	aca	σca	aat	qca	cqc	caa	raa	aag	gga	gaa	acg	cgc	ctt	541
Val	Ile	Ile	Thr	Ala	Glv	Ala	Ara	Gln	Xaa	Lys	Gly	Glu	Thr	Arg	Leu	
		110			1		115			-2-	2	120		-		
225	tta		Car	CCS	225	ata		atc	ttc	aag	tta		att	tcc	agt	589
100	Lou	Y 2 2	Cla	2	245	77-1	Ala	Ile	Dhe	Lve	Leu	Met	Tle	Ser	Ser	•
ASII		Ndd	GIII	Arg	ASII	130	MIG	116	FIIC	шys	135	1100				
	125											a++	+00	224	cca	637
att	gtc	cag	tac	agc	CCC	cac	tgc	aaa	ctg	all.	Tla	yet	602	Acn	Dro	037
	val	GIN	lyr	ser		HIS	Cys	Lys	Leu		irre	vai	261	Maii	155	
140					145					150						685
gtg	gat	atc	tta	act	tat	gta	gct	tgg	aag	ttg	agt	gca	בבב	CCC	aaa	005
Val	Asp	Ile	Leu		Tyr	Val	Ala	Trp		Leu	Ser	Ala	Pne	PIO	гуя	
				160					165			1.		170		~~~
aac	cgt	att	att	gga	agc	ggc	tgt	aat	ctg	ata	mhg	gct	cgt	ttt	cgt	733
Asn	Arg	Ile	Ile	Gly	Ser	Gly	Cys	Asn	Leu	Ile	Xaa	Ala	Arg	Phe	Arg	
			175					180					185			
ttc	ttg	att	gga	caa	aag	ctt	ggt	atc	cat	tct	gaa	agc	tgc	cat	gga	781
Phe	Leu	Ile	Gly	Gln	Lys	Leu	Gly	Ile	His	Ser	Glu	Ser	Cys	His	Gly	
		190	-		•		195					200				
taa	atc	ctc	gga	gag	cat	qqa	qac	tca	agt	gtt	cct	gtg	tgg	agt	gga	829
Trp	Ile	Leu	Glv	Glu	His	Glv	Asp	Ser	Ser	Val	Pro	Val	Trp	Ser	Gly	
	205					210	•				215					
ata		ata	act	aat	atc		tta	aaq	gat	cta	aac	tct	qat	ata	gga	877
Val	Acn	Tle	Ala	Glv	Val	Pro	Len	Lvs	Asp	Leu	Asn	Ser	Ast	Ile	Gly	
220	N3.11		AI G	G ₁ ,	225			-,-		230					235	
						<b>C33</b>	+ 00	- 222	22+				gaa	ato	act	925
act mb-	gat	ddd	gat	200	gag	Caa	~~ <u>~</u>	Tura	nac Nan	1751	. cac	Tyc	Gli	Val	Thr	
Inr	Asp	Lys	Asp		GIU	GIN	rrp	гуз			nıs	Lys	GIC	250	Thr	
				240					245							973
gca	act	gcc	tat	gag	att	att	aaa	atg	aaa	ggt	tat	act	. CCT	. cg	gcc	3/3
Ala	Thr	Ala	Tyr	Glu	Ile	Ile	Lys			Gly	Tyr	Thr			Ala	
			255					260					265			
att	ggc	cta	tct	gtg	gcc	gat	. tta	aca	gaa	agt	att	ttg	aag	g aa	tctt	1021
Ile	Gly	Leu	Ser	Val	Ala	Asp	Leu	Thr	Glu	Ser	: Ile	e Leu	Ly:	s As	n Leu	
	-	270				-	275					280				
add	aga			cca	att	tcc	acc	ata	act	aac	gge	cto	ta	t gg	a ata	1069
Ara	Ara	Jle	His	Pro	Val	Ser	Thr	Ile	Thi	Lv	Giv	/ Let	Ty	r Gl	y Ile	
3	285					290				- 4	29	5	•			
rat			_ ~ - ~	. ++-	. ~+~				- +a	ato			a aa	a aa	c ggt	1117
1 d L	944	944	. y.d	Dh-	Tan	Car	- T12	- D-	3'	. T1	a Te	r GJ/	, GJ	u As	n Gly	
		910	, val	. rne			. 110		- Cy:	31			,		315	
300					305							a (72)	a (12)	a ac		
att	acc	<b>a</b> a.c	: ככנ	. ata	aag	ata	a dd		acc		- ga	. ga	. ga	ומיו	c cat	
ile	Thr	AST	ı Leu	ı ile	: rys	: 116	- Ly:	s rei	a I.U.	PI	י עניי	u 011	u 01	~ ^1	a His	

770	
320 325 330	
ctg aaa aaa agt gca aaa aca ctc tgg gaa att cag aat aag ctt aag	1213
Leu Lys Lys Ser Ala Lys Thr Leu Trp Glu Ile Gln Asn Lys Leu Lys	
335 340 345	
ctt taaagttgcc taaaactacc attccgaaat tattgaagag atcatagata	1266
Leu	
caggattata taacgaaatt ttgaataaac ttgaattcct aaaagatgga aacaggaaag	1226
	1326
taggtagagt gattttccta tttatttagt cctccagctc ttttattgag catccacgtg	1386
ctggacgata cttatttaca attcckaagt atttttggta cctctgatgt agcagcactt	1446
gccatgttat atatatgtag ttgrmatttg gttcccaaaa agtaggatgt aggtatttat	1506
tgtgttctag aaattccgac tcttttcatt agatatatgc tatttctttc attcttgctg	1566
gtttatacct atgttcattt atatgctgta aaaaagtagt agcttcttct acaatgtaaa	1626
aataaatgta catacaaaaa aaaaaamcmc	1656
·	
	*
<210> 308	
<211> 517	
<212> DNA	
<213> Homo sapiens	-
ters to the copy of the copy o	
220.	
<220>	
<221> CDS	
<222> 48164	
<221> sig_peptide	
<222> 4889	
<223> Von Heijne matrix	
score 4	
30010 4	
CAC VVMICI PRO TEC / DU	
seq YYMVCLFFRLIFS/EH	
<221> polyA_signal	
<221> polyA_signal	
<221> polyA_signal <222> 482487	
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487 &lt;221&gt; polyA_site</pre>	
<221> polyA_signal <222> 482487	
<221> polyA_signal <222> 482487 <221> polyA_site <222> 505517	
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482. 487  &lt;221&gt; polyA_site &lt;222&gt; 505. 517 &lt;400&gt; 308</pre>	
<221> polyA_signal <222> 482. 487  <221> polyA_site <222> 505. 517  <400> 308 aggagatage ctegtagaaa tgacaaccac aatgttaata ctaacat atg tat tac	56
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482. 487  &lt;221&gt; polyA_site &lt;222&gt; 505. 517  &lt;400&gt; 308 aggagatage ctegtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr</pre>	
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482. 487  &lt;221&gt; polyA_site &lt;222&gt; 505. 517  &lt;400&gt; 308 aggagatage ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac</pre>	56
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482. 487  &lt;221&gt; polyA_site &lt;222&gt; 505. 517  &lt;400&gt; 308 aggagatage ctegtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr</pre>	
<221> polyA_signal <222> 482. 487  <221> polyA_site <222> 505. 517  <400> 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tac	
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tae</pre>	104
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tae</pre>	
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tae</pre>	104
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tae</pre>	104
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482. 487  &lt;221&gt; polyA_site &lt;222&gt; 505. 517  &lt;400&gt; 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tae</pre>	104
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tae</pre>	104
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482. 487  &lt;221&gt; polyA_site &lt;222&gt; 505. 517  &lt;400&gt; 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tae</pre>	104
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482. 487  &lt;221&gt; polyA_site &lt;222&gt; 505. 517  &lt;400&gt; 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tae</pre>	104
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatage etegtagaaa tgacaaceae aatgttaata etaacat atg tat tae</pre>	104 152 204
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac</pre>	104 152 204 264 324
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatage ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac</pre>	104 152 204 264 324 384
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac</pre>	104 152 204 264 324 384 444
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatage ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac</pre>	104 152 204 264 324 384 444 504
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 482487  &lt;221&gt; polyA_site &lt;222&gt; 505517  &lt;400&gt; 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac</pre>	104 152 204 264 324 384 444

<210> 309 <211> 405 <212> DNA

<213> Homo sapiens

```
<220>
<221> CDS
<222> 185..334
<221> sig_peptide
<222> 185..295
<223> Von Heijne matrix
      score 5.90000009536743
      seq LSYASSALSPCLT/AP
<221> polyA_signal
<222> 355..360
<221> polyA_site
<222> 392..405
<400> 309
atcacettet tetecateet tstetgggee agtececare ceagtecete teetgacetg
cccagcccaa gtcagccttc agcacgcgct tttctgcaca cagatattcc aggcctacct
                                                                     120
ggcattccag gaceteegma atgatgetee agtecettae aagegettee tggatgaggg
                                                                     180
                                                                     229
tggc atg gtg ctg acc acc ctc ccc ttg ccc tct gcc aac agc cct gtg
     Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val
                                 -30
             -35
aac atg ccc acc act ggc ccc aac agc ctg agt tat gct agc tct gcc
                                                                     277
Asn Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala
                            -15
                                                -10
                                                                      325
ctg tcc ccc tgt ctg acc gct cca aag tcc ccc cga ctt gct atg atg
Leu Ser Pro Cys Leu Thr Ala Pro Lys Ser Pro Arg Leu Ala Met Met
   - 5
cct gac aac taaatatcct tatccaaatc aataaarwra raatcctccc
                                                                      374
Pro Asp Asn
                                                                      405
tccaraaggg tttctaaaaa caaaaaaaaa a
<210> 310
<211> 1087
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 195..347
<221> sig_peptide
<222> 195..272
<223> Von Heijne matrix
      score 7.09999990463257
      seq LASLQWSLTLAWC/GS
<221> polyA_signal
<222> 1037..1042
<221> polyA_site
<222> 1071..1082
<400> 310
aaagtgtaga acacggacct ctgagttatg ctcttgagag gtgccaaagc tgggctgttt
                                                                        60
acctacetta tecacagage tetgaaagte aagecagaaa ggaaggatte caaattettg
                                                                       120
gaattttatc tagaaaagaa gactaagcag cttttgttct tctgtgaccc agttgctggc
                                                                       180
ccaagacatg gaca atg acc ccc tgg tgt ttg gcg tgt ctg ggg agg agg
```

Met Thr Pro Trp Cys Leu Ala Cys Leu Gly Arg Arg

-25 -20 -15	
cet etc get tet ttg cag tgg age etg aca etg geg tgg tgt gge tee	278
Pro Leu Ala Ser Leu Gln Trp Ser Leu Thr Leu Ala Trp Cys Gly Ser	
-10 -5 1	
gge age cae tgg aca gag aga coa akt cag akt tea ceg tgg akt tet	326
Gly Ser His Trp Thr Glu Arg Pro Xaa Gln Xaa Ser Pro Trp Xaa Ser	320
5 10 15 The Aug 110 Aug 110 Aug 110 Aug 110 The Aug 11	
ctg toa gcg acc acc agg ggg tgatcacacg gaaggtgaac atccaggtcg	377
Leu Ser Ala Thr Thr Arg Gly	3,,,
20 25	
gggatgtgaa tgacaacgcg cccacatttc acaatcagcc ctacagcgtc cgcatccctg	437
araatacacc agtggggacg cocatcitica togtgaatgc cacagacccc gacttggggg	497
cagggggcag cgtcctctac teettecage ceceeteeca attettegee attgacageg	557
	617
cccgcggtat cktcacagtg atccgggagc tggactacga taccacremg gcctaccagc tcwcggtcwa cgccacagat caagacaara ccaggcctct gcccaccstg gccaacttgg	677
ccatcatcat cacagatgto caggacatgg accocatctt catcaacctg cottacagca	737
ccaacateta cgagcattet ceteegggea cgaeggtgeg cateateace gecatagace	797
	857
aggataaagg acgtccccgg ggcattggct acaccatcgt ttcagggcat ctgtgtttac	917
aagaacccaa gateteteag gageteagga aaaggggett getgtgagge teagggttee	977
catggacatt ctgagetgac ceteetcage attggatete etggetcagg aactaggaac	1037
gaagettgga tgttttetee ttteetacag catetgtatt cattteetat agttgecata	1037
ataaaatgcc actaacttag tggcttaaaa accaaaaaaa aaaaaccctt	1007
^^^	
<210> 311	
<211> 916	
<212> DNA	
<213> Homo sapiens	
•••	
<220>	
<221> CDS	
<222> 90815	
<221> sig_peptide	
<222> 90179	
<223> Von Heijne matrix	
score 13.1999998092651	
seq LLLLSTLVIPSAA/AP	
<221> polyA_signal	
<222> 883888	
<221> polyA_site	
<222> 905916	
<400> 311	
aaaacagtac gtgggcggcc ggaatccggg agtccggtga cccgggctgt ggtctagcat	60
aaaggcggag ccagaagaag gggcggggt atg gga gaa gcc tcc cca cct gcc	113
Met Gly Glu Ala Ser Pro Pro Ala	
-30 -25	
ccc gca agg cgg cat ctg ctg gtc ctg ctg ctc ctc tct acc ctg	161
Pro Ala Arg Arg His Leu Leu Val Leu Leu Leu Leu Ser Thr Leu	
-20 -15 -10	
gtg atc ccc tcc gct gca gct cct atc cat gat gct gac gcc caa gag	209
gtg ate eee tee get ged get eet die eat gat get gat get edd gag	
Val Ile Pro Ser Ala Ala Ala Pro Ile His Asp Ala Asp Ala Gln Glu	
	257
age tee ttg ggt ete aca gge ete cag age eta ete caa gge tte age	23/
Ser Ser Leu Gly Leu Thr Gly Leu Gln Ser Leu Leu Gln Gly Phe Ser	
15 20 25	
and one are one are are organic organic and ago the the	
ega ett tte etg aaa ggt aac etg ett egg gge ata gae age tta tte	305

Arg	Leu	Phe	Leu 30	ГХа	Gly	Asn	Leu	Leu 35	Arg	Gly	Ile	Asp	Ser 40	Leu	Phe	
tct	gcc	ccc	atq	gac	ttc	caa	qqc	ctc	cct	aga	aac	tac	cac	aaa	gag	353
	Āla		_	-												
		45		<b>F</b>		5	50			,		55		-7-		
a 2 a	aac		~~~	636	c	cta		226	220	200			300		at a	401
																401
GIU	Asn	GIN	GIU	HIS	GIR		GIY	ASII	Asn	Thr		Ser	ser	HIS	Leu	
	60					65					70					
	atc															449
Gln	Ile	Asp	Lys	Met	Thr	Asp	Asn	Lys	Thr	Gly	Glu	Val	Leu	Ile	Ser	
75					80					85					90	
gag	aat	ata	ata	gca	tcc	att	caa	cca	vca	gag	aaa	anc	ttc	gag	gat	497
	Asn															
014	7.511	141	• • •				<b></b>		100	GIG	Gly	Add	F11C	105	017	
				95												
	ttg															545
Asp	Leu	Lys	Val	Pro	Arg	Met	Glu	Glu	Lys	Glu	Ala	Leu	Val	Pro	Xaa	
			.110					115					120			
car	aay	gcc	acg	gac	agc	ttc	CAC	aça	gaa	ctc	cat	ccc	cgg	gtg	gcc	593
Gln	Lys	Āla	Thr	Asp	Ser	Phe	His	Thr	Glu	Leu	His	Pro	Arg	Val	Ala	
	•	125		•			130					135				
ttc	tgg		att	220	cta	cca		caa	agg	tcc	Cac		gat	acc	cta	641
	Trp			-	_							_	•	-	_	•••
FIIC	-	116	116	гуя	neu		Arg	Arg	ALG	SEI		GIII	Asp	Ala	neu	
	140					145					150					
	ggc						_	_	_		_	_	_	-		689
Glu	Gly	Gly	His	Trp	Leu	Xaa	Glu	Lys	Arg	His	Arg	Leu	Gln	Ala	Ile	
155					160					165					170	
caa	gat	qqa	ctc	cqc	aaq	qqq	acc	cac	aaq	gac	rtc	cta	daa	rag	ggg	737
	Asp															
5	_P	,		175	-1-	,,			180					185	1	
	gar						200								++=	785
	-	-						_			•					703
inr	Glu	ser		ser	HIS	Ser	Arg		Ser	Pro	Arg	гуя		ura	геп	
			190					195					200			
ctg	tac	atc	ctc	arg	CCC	tct	cgg	cag	ctg	tar	gggt	999 ·	gacc	<b>3</b> 999	ar	835
Leu	Tyr	Ile	Leu	Xaa	Pro	Ser	Arg	Gln	Leu							
	-	205					210									
mac	ctac	ta 1	tage	cccc	at c	arac	ccta	c cc	caad	cacc	ata	taga	aat	aaa¤	ttcttt	895
	acat	-	_				5		3			- 33**		3		916
	acati	-ca	aaaa	2000	aa a											720

<210> 312

<211> 583

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 52..513

<221> sig_peptide <222> 52 .231

<223> Von Heijne matrix score 4
seq LVRRTLLVAALRA/WM

<221> polyA_signal

<222> 553..558

<221> polyA_site <222> 572..583

<400> 312

aaggaaacag caaccagagg gagatgatca cotgaaccao tgctocaaao o atg ggo Met Gly -60	57
agt aaa tgc tgt aaa ggt ggt cca gat gaa gat gca gta gaa aga cag Ser Lys Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu Arg Gln -55 -50 -45	105
agg cgg cag aag ttg ctt ctt gca caa ctg cat cac aga aaa agg gtg Arg Arg Gln Lys Leu Leu Ala Gln Leu His His Arg Lys Arg Val -40 -35 -30	153
aar gca gct ggg cag atc cag gcc tgg tgg cgt ggg gtc ctg gtg cgc Lys Ala Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu Val Arg -25 -20 -15	201
agg acc ctg ctg gtt gct gcc ctc agg gcc tgg atg att cag tgc tgg Arg Thr Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln Cys Trp -10 -5 1 5	249
tgg agg acg ttg gtg cag aga cgg atc cgt cag cgg cgg cag gcc ctg Trp Arg Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln Ala Leu 10 15 20	297
ttr ggg gtc tac gtc atc cag gag cag gcg gtc aag ctc cag tcc Leu Gly Val Tyr Val Ile Gln Glu Gln Ala Ala Val Lys Leu Gln Ser 25 30	345
tgc atc cgc atg tgg cag tgc cgg caa tgt tac cgc caa atg tgc aat Cys Ile Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met Cys Asn 40 45 50	393
get etc tge ttg tte cag gte cea aaa age age ett gee tte caa act Ala Leu Cys Leu Phe Gln Val Pro Lys Ser Ser Leu Ala Phe Gln Thr 55 60 65 70	441
gat ggc ttt tta cag gtc caa tat gca atc cct tca aag cag cca gag Asp Gly Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln Pro Glu 75 80 85	489
ttc cac att gaa atc cta tca atc tgaaaggcct ggggcatgga gaacaggctg Phe His Ile Glu Ile Leu Ser Ile 90	543
cactacccta ataaatgtct gaccaggtaa aaaaaaaaaa	583
<210> 313 <211> 697	
<212> DNA <213> Homo sapiens	
<220> <221> CDS	
<222> 172438	_
<221> sig_peptide	
<222> 172354 <223> Von Heijne matrix	
score 4.69999980926514 seq LLPCNLHCSWLHS/SP	
<221> polyA_signal <222> 682687	
<221> polyA_site <222> 685697	

agattggctg ggcagatggg ctgactggct gggcagatgg gtgggtgagt tccctctccc cagagccatc ggccaggtac caaagctcag ctgtatggat tcccaacagg aggacctgcg cttccctggg acccattgtt gtactggatt aacaagcgac ggcgctacgg c atg aat

120 177

<400> 313

Met Asn	
-60 gca gcc atc aac acg ggc cct gcc cct gct gtc acc aaq act gag act	225
Ala Ala Ile Asn Thr Gly Pro Ala Pro Ala Val Thr Lys Thr Glu Thr	223
-55 -50 -45	272
gag gtc cag aat cca gat gtt ctg tgg gat ttg gac atc ccc gaa gcc Glu Val Gln Asn Pro Asp Val Leu Trp Asp Leu Asp Ile Pro Glu Ala	273
-40 -35 -30	
agg age cat get gae caa gae age aae eee aag geg gaa gee etg ete	321
Arg Ser His Ala Asp Gln Asp Ser Asn Pro Lys Ala Glu Ala Leu Leu -25 -20 -15	
ccc tgc aac ctg cac tgc agc tgg ctc cac agc agc ccc agg cca gat	369
Pro Cys Asn Leu His Cys Ser Trp Leu His Ser Ser Pro Arg Pro Asp -10 -5 1 5	
ccc cat tee cae tte cca tet kte agg agg tge cet ttg eee cae cet	417
Pro His Ser His Phe Pro Ser Xaa Arg Arg Cys Pro Leu Pro His Pro	
10 15 20 tgt gca acc tac ecc ecs kgc tgaaccacte tgteteetat cetttggeca	468
Cys Ala Thr Tyr Pro Pro Xaa  25	400
cctgtcctga aaggaatgtt ctcttccatt ccctcctgaa tctggcccag gaagaccata	528
gcttcaatgy caagcctttt ccttcaaaac tgtagcctcc tctcactgaa ggtgggagct	588
gcaggaatca ggtgcagagt aggaaatgga actaacctca ggaaggtggt attgacagag	648
gtcaggaccc acctggatgt catgctatga aacattaaaa gaaaaaaaa	697
<210> 314	
<211> 803	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 148366	
<221> sig_peptide	
<222> 148225	
<223> Von Heijne matrix	
score 5.5	
seq LFTLLFLIMLVLK/LD	
<221> polyA signal	
<222> 770775	
<221> polyA_site	
<222> 792803	
<400> 314	
aaatgggggg aaaagggcgg aaaaggacaa ggatccaaac tggcgaattt gctgatcttc	60
gegteeetet eegettteeg geeggeageg etgeeagggt atatteett tetteegate	120
ctgcaacago ototttaaac tgtttaa atg aga atg too ttg got cag aga gta	174
Met Arg Met Ser Leu Ala Gln Arg Val	
-25 -20	222
cta ctc acc tgg ctt ttc aca cta ctc ttc ttg atc atg ttg gtg ttg Leu Leu Thr Trp Leu Phe Thr Leu Leu Phe Leu Ile Met Leu Val Leu	266
-15 -10 -5	
aaa ctg gat gag aaa gca cct tgg aac tgg ttc ctc ata ttc att cca	270
Lys Leu Asp Glu Lys Ala Pro Trp Asn Trp Phe Let Ile Phe Ile Pro	
1 5 10 15	
gto tgg ata tit gat act ato off off gto off off att gtg aaa atg	318
Val Trp Ile Phe Asp Thr Ile Leu Leu Val Leu Leu Ile Val Lys Met	

20

25

```
get ggg egg tgt aag tet gge ttt gae ete gae atg gat eac aca ata
                                                                     366
Ala Gly Arg Cys Lys Ser Gly Phe Asp Leu Asp Met Asp His Thr Ile
                                40
taaaaaaaa aacctggtac ctcattgcac tgtkacttaa attasccttc tgcctcgcac
                                                                     426
totgtgctaa actggaacag tttactacca tgaatctatc ctatgtcttc attcctttat
                                                                     486
gggccttgct ggctggggct ttaacagaac tcggatataa tgtctttttt gtgaaagact
                                                                     546
gacttctaag tacatcatct cctttctatt gctgttcaac aagttaccat taaagtgttc
                                                                     606
tgaatctgtc aagcttcaag aataccagag aactgaggga aaataccaaa tgtagtttta
tactacttcc ataaaacagg attggtgaat cacggacttc tagtcaacct acagcttaat
                                                                     726
tattcagcat ttgagttatt gaaatcctta ttatctctat gtaaataaag tttgttttgg
                                                                     786
acctcaaaaa aaaaaaa
                                                                     803
<210> 315
<211> 823
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 175..336
<221> sig_peptide
<222> 175..276
<223> Von Heijne matrix
      score 3.70000004768372
      seg SVLNVGHLLFSSA/CS
<221> polyA_site
<222> 812..823
<400> 315
aaggegegeg egaceggegg etetttggeg eggattaggg ggteteggeg agggagteat
                                                                      60
caagetttgg tgtatgtgtt ggccggttct gaagtettga agaagetetg etgaggaaga
                                                                     120
                                                                     177
ccaaagcagc actogttgcc aattagggaa tggaccgttt gggttccttt agca atg
                                                                     225
atc cct ctg ata age cac ctt gee gag get get cct cet acc tea tgg
Ile Pro Leu Ile Ser His Leu Ala Glu Ala Ala Pro Pro Thr Ser Trp
           -30
                                -25
ago ott ata toa agt gtg etg aat gtg ggo cac oto ott tit too tot
                                                                      273
Ser Leu Ile Ser Ser Val Leu Asn Val Gly His Leu Leu Phe Ser Ser
                                                - 5
        -15
                            -10
get tge agt gtt tea etc gag get ttg agt aca aga aac atc aaa geg
Ala Cys Ser Val Ser Leu Glu Ala Leu Ser Thr Arg Asn Ile Lys Ala
                                        10
    1
atc ata ctt atg aaa taatggcttc agattttcct gtccttgatc ccagctggac
                                                                      376
Ile Ile Leu Met Lys
                20
tgctcaagaa raaatggccc ttttagaasc tgtgatggac tgtggctttg gaaattggca
                                                                      496
ggatgtagcc aatcaaatgt gcaccaarac caaggaggag tgtgagaagc actatatgaa
                                                                      556
quatttcatc aataacceye tgtttgcatc trscctgctg aacctgaaac aascagrgga
agcaaaaact gctgacacag ccattccatt tcactctaca ratgaccctc cccgacckac
                                                                      676
ctttgactcc ttgctttctc gggacatggc cgggtacwtg ccmgctcgag cagatttcat
tgaggaattt gacaattatg cagaatggga cttgagagac attgattttg ttgaagatga
                                                                      736
                                                                      796
ctcqqacatt ttacatqctc tgaagatggc tgtggtagat atctatcatt ccaggttaaa
                                                                      823
ggagagacaa agacgaaaaa aaaaaaa
```

823

```
<211> 823
<212> DNA
```

<213 > Homo sapiens

<220>

<221> CDS

<222> 191..553

<221> sig_peptide

<222> 191..304

<223> Von Heijne matrix score 5.69999980926514 seq LAFLSCLAFLVLD/TQ

<221> polyA_signal

<222> 766..771

<221> polyA_site

<222> 804..817

## <400> 316

aactotgoag ggcotocaag gocaggotto agggotggga otcagtootg aggcactggg gagccatgag gggctgtggc agggagggc agggtgtgga aagactcccc tggggccatg 120 gtggagatgt getgaggtet tetecetgat egtettetee teeetgetga eegaeggeta 180 ccagaackag atg gag tot ccg cag oto cac tgc att oto aac agc aac 229 Met Glu Ser Pro Gln Leu His Cys Ile Leu Asn Ser Asn -35 -30 age gtg gee tge age ttt gee gtg gga gee gge tte etg gee tte etc 277 Ser Val Ala Cys Ser Phe Ala Val Gly Ala Gly Phe Leu Ala Phe Leu -20 -15 age tge etg gee tte ete gte etg gae aca eag gag ace ege att gee 325 Ser Cys Leu Ala Phe Leu Val Leu Asp Thr Gln Glu Thr Arg Ile Ala -5 ggc acc ege tte aag aca gee tte eag ete etg gae tte ate etg get 373 Gly Thr Arg Phe Lys Thr Ala Phe Gln Leu Leu Asp Phe Ile Leu Ala 15 gtt ctc tgg gca gtt gtc tgg ttc atg ggt ttc tgc ttc ctg gcc aac 421 Val Leu Trp Ala Val Val Trp Phe Met Gly Phe Cys Phe Leu Ala Asn 30 35 caa tgg cag cat tcg ccg ccc aaa gar kkc ctc ctg ggg agc agc agt 469 Gln Trp Gln His Ser Pro Pro Lys Glu Xaa Leu Leu Gly Ser Ser Ser 45 50 gcc cag gca gcc atc ggc stt cac ctt ctt ctc cat cct tgt ctg gat 517 Ala Gln Ala Ala Ile Gly Xaa His Leu Leu Leu His Pro Cys Leu Asp 60 65 att cca rgc cta cct ggc akk cca gga cct ccg aaa tgatgctcca 563 Ile Pro Xaa Leu Pro Gly Xaa Pro Gly Pro Pro Lys gtcccttacm arcgcttcct ggatgaaggt ggcatggtqs kkaacaccct ccccttqccc 623 tctgccaaca gcctgtgaac atgcccacca ctggccccaa cagcctgagt tatgctagct 683 ctgccctgtc cccctgtctg accgctcmaa agtccccccg gcttgctatg atgcctgaca 743 actaaatatc cttatccaaa tcaataaaga gagaatcctc cctccagaag ggtttctaaa 803 aacaaaaaa aaaahncctt

-233-

<210> 317

<211> 1112

<212> DNA

<213 > Homo sapiens

agggattgcg aatcctccqc tgaggtgatt tggatatccc taqaacqttq aqqqcacqaq 60 tegggteetg agaccaggte etcagecage agagecaegt teett atg age ace gtg 117 Met Ser Thr Val ggt tta ttt cat ttt cct aca cca ctg acc cga ata tgc ccg gcg cca 165 Gly Leu Phe His Phe Pro Thr Pro Leu Thr Arg Ile Cys Pro Ala Pro -25 -30 tgg gga ctc cgg ctt tgg gag aag ctg acg ttg tta tcc cca gga ata 213 Trp Gly Leu Arg Leu Trp Glu Lys Leu Thr Leu Leu Ser Pro Gly Ile -15 -10 gct gtc act ccg gtc cag atg gca ggc aag aag gac tac cct gca ctg 261 Ala Val Thr Pro Val Gln Met Ala Gly Lys Lys Asp Tyr Pro Ala Leu 10 ctt tcc ttg gat gag aat gaa ctc gaa gag cag ttt gtg aaa gga cac 309 Leu Ser Leu Asp Glu Asn Glu Leu Glu Glu Gln Phe Val Lys Gly His 20 25 ggt cca ggg ggc cag gca acc aac aaa acc agc aac tgc gtg gtg ctg 357 Gly Pro Gly Gly Gln Ala Thr Asn Lys Thr Ser Asn Cys Val Val Leu 35 40 405 aar mac atc ccc tca ggc atc gtt gta aag tgc cat cag aca aga tca Lys Xaa Ile Pro Ser Gly Ile Val Val Lys Cys His Gln Thr Arg Ser 50 55 60 gtt gat cag aac aga aag cta gct cgg aaa atc cta caa gag aaa gta 453 Val Asp Gln Asn Arg Lys Leu Ala Arg Lys Ile Leu Gln Glu Lys Val 70 75 rat gtt ttc tac aat ggt gaa aac agt cct gtt cac aaa gaa aaa cga 501 Xaa Val Phe Tyr Asn Gly Glu Asn Ser Pro Val His Lys Glu Lys Arg 549 gaa gcg gcg aag aaa aaa car gaa agg aaa aaa aga gca aag gaa acc Glu Ala Ala Lys Lys Gln Glu Arg Lys Lys Arg Ala Lys Glu Thr 100 105 597 ctg gaa aaa aag aas ctm ctt aaa raa ctg tgg gag tca agt aaa aag Leu Glu Lys Lys Xaa Leu Leu Lys Xaa Leu Trp Glu Ser Ser Lys Lys 115 120 653 gtc cac tgagaaaaga attagagatt ccaactgaca gaatctgcca gaagctccca Val His gggaataatg gtggcgagtt ccatcaccag cattattata gtgcttcaaa agaaatattt 713 773 ttgatgaact taaaagacaa caaatttatt taaatggtgc actaaactgt agtgaacaga 833 gacatgcacg attcaagaat aaaactcggc cgggcacggt ggacggtgcc tcacatctgt 893 aatcccagca ctttgggagg ccgaggcggg cggatcactt gaggtcagga gtttgagacc 953 agcctggcca acatggtgaa accccgtctc tactaaaaat acaaaaaatt agccaggcat ggtggcgggc acctgtaatc ccagctactc gggaggccga ggcaggagaa ttgcgtgaac 1013 1073 ctgggaggcg gaggttgcag tgagctgaga tcgcgccact gcactcaagc ctgggcaaca cctgggtgac agagcaagac cccatcycaa aaaaaaaaa 1112

-234-

<210> 318 <211> 1623

WO 99/31236 -235- PCT/IB98/02122

```
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 47..586
<221> sig_peptide
<222> 47..124
<223> Von Heijne matrix
     score 6.30000019073486
     seg GVGLVTLLGLAVG/SY
<221> polyA_signal
<222> 1583..1588
<221> polyA_site
<222> 1614..1623
<400> 318
                                                                      55
agggatotgt oggottgtca ggtggtggag gaaaaggogo toogto atg ggg atc
                                                   Met Gly Ile
                                                       -25
cag acg age eee gte etg etg gee tee etg ggg gtg ggg etg gte act
                                                                     103
Gln Thr Ser Pro Val Leu Leu Ala Ser Leu Gly Val Gly Leu Val Thr
           -20
                                -15
ctg ctc ggc ctg gct gtg ggc tcc tac ttg gtt cgg agg tcc cgc cgg
                                                                     151
Leu Leu Gly Leu Ala Val Gly Ser Tyr Leu Val Arg Arg Ser Arg Arg
       - 5
                            1
cct cag gtc act ctc ctg gac ccc aat gaa aag tac ctg cta cga ctg
                                                                     199
Pro Gln Val Thr Leu Leu Asp Pro Asn Glu Lys Tyr Leu Leu Arg Leu
                                        20
                    15
cta gac aag acg act gtg agc cac aac acc aag agg ttc cgc ttt gcc
                                                                     247
Leu Asp Lys Thr Thr Val Ser His Asn Thr Lys Arg Phe Arg Phe Ala
                30
                                    35
ctg ccc acc gcc cac cac act ctg ggg ctg cct gtg ggc aaa cat atc
                                                                     295
Leu Pro Thr Ala His His Thr Leu Gly Leu Pro Val Gly Lys His Ile
          45
                                50
                                                                      343
tac ctc tcc acm mga att gat ggc agc ctg gtc atc agg cca tac act
Tyr Leu Ser Thr Arg Ile Asp Gly Ser Leu Val Ile Arg Pro Tyr Thr
                            65
cct gtc acc agt gat gag gat caa ggc tat gtg gat ctt gtc mtc aag
                                                                      391
Pro Val Thr Ser Asp Glu Asp Gln Gly Tyr Val Asp Leu Val Xaa Lys
                                            85
                        80
gto tac ctg aag ggt gtg cac ccc aaa ttt cct gag gga ggg aar atg
Val Tyr Leu Lys Gly Val His Pro Lys Phe Pro Glu Gly Gly Lys Met
                     95
                                        100
tot cak tac ctg gat asc ctg aaa gtt ggg gat btg gtg gaa ttt csg
                                                                      487
Ser Xaa Tyr Leu Asp Xaa Leu Lys Val Gly Asp Xaa Val Glu Phe Xaa
                                    115
                110
ggg cca agc ggg ttg ctc act tac act gga aaa ggg cat ttt aac att
Gly Pro Ser Gly Leu Leu Thr Tyr Thr Gly Lys Gly His Phe Asn Ile
                                                     135
                                130
            125
cag ccc aac aag aat ctc cac cag aac ccc gag tgg cga aga aac tgg
                                                                      583
Gln Pro Asn Lys Asn Leu His Gln Asn Pro Glu Trp Arg Arg Asn Trp
                             145
                                                150
                                                                      636
gaa tgattgccgg cgggacagga atcaccccaa tgctacagct gatccgggcc
atcctgaaag tccctgaaga tccaacccag tgctttctgc tttttgccaa ccagacagaa
                                                                      696
                                                                      756
aaggatatca tottgoggga ggacttagag gaactgoagg cocgotatoo caatogottt
aagetetggt teactetgga teatececca aaagrttggg eetacageaa gggetttgtg
                                                                       816
actgccgacw tgatccggga acacctgccc gctccagggg atgatgtgct ggtactgctt
```

tgtgggccmc ccccaatggt gcagctggcc tgccatccca acttggacaa actgggctac

936

9.0 \$4.0

. :

```
tcacaaaaga tgcgattcac ctactgagca tcctccagct tccctggtgc tgttcgctgc
                                                                     996
agttgttccc catcagtact caagcactak aagcettagr ktcctktcct cagagtttca
                                                                    1056
ggttttttca gttrsatcka gagctgaaat ctggatagta cctgcaggaa caatattcct
                                                                    1116
gtagccatgg aagagggcca aggctcagtc actccttgga tggcctccta aatctccccg
                                                                    1176
                                                                    1236
tggcaacagg tccaggagag gcccatggag cagtetette catggagtaa gaaggaaggg
agcatgtacg cttggtccaa gattggctag ttccttgata gcatcttact ctcaccttct
                                                                    1296
ttgtgtctgt gatgaaagga acagtctgtg caatgggttt tacttaaact tcactgttca
acctatgage aaatetgtat gtgtgagtat aagttgagea tageataett ecagaggtgg
                                                                    1416
tcttatggag atggcaagaa aggaggaaat gatttcttca gatctcaaag gagtctgaaa
                                                                    1476
tatcatattt ctgtgtgtgt cdctctcagc ccctgcccad gctagaggga wacagctact
                                                                    1536
                                                                    1596
gataatcgaa aactgctgtt tgtgggcarg aacccctggc tgtgcaaata atggggctga
                                                                    1623
ngccctgtgt gatattgaaa aaaaaaa
<210> 319
<211> 526
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 99..371
<221> sig peptide
<222> 99..290
<223> Von Heijne mátrix
      score 3.7999995231628
      seg LFIVVCVICVTLN/FP
<221> polyA signal
<222> 491..496
<221> polyA_site
<222> 513..524
<400> 319
attggattag tagaattgct tttgtcattc cattgttttc atatatttgt ttgggacatt
                                                                       60
ttactttttt ctgttaacgc ttaccctagr aattagaa atg aca cca cgt att ctt
                                                                      116
                                          Met Thr Pro Arg Ile Leu
                                                                      164
age gaa gte eag ttt tea gea ttt tgt eet tat tgg aca ata gea agg
Ser Glu Val Gln Phe Ser Ala Phe Cys Pro Tyr Trp Thr Ile Ala Arg
                                                     -45
            -55
                                 -50
ata tta gaa cgt gtt ggt tcc gcg tgc ttc cgt ctt gag tta tgt gct
                                                                       212
Ile Leu Glu Arg Val Gly Ser Ala Cys Phe Arg Leu Glu Leu Cys Ala
                             -35
                                                                       260
gct att gtc gga tat ttt gtc tta gat gta cgt act ttc ctg ttc att
Ala Ile Val Gly Tyr Phe Val Leu Asp Val Arg Thr Phe Leu Phe Ile
    -25
                         -20
                                             -15
                                                                       308
gtg gta tgt gta att tgc gtt act ttg aat ttt cca cgt ttt tac ttt
Val Val Cys Val Ile Cys Val Thr Leu Asn Phe Pro Arg Phe Tyr Phe
ctt tgt ctc tca tca ctt acc gct ttt ggg acc ccc ccc atc ggg gtt
                                                                       356
Leu Cys Leu Ser Ser Leu Thr Ala Phe Gly Thr Pro Pro Ile Gly Val
                                 15
                                                     20
            10
                                                                       411
cac att ccc tct ccc tararcacac tcccttggat ttcctcradt ggggtctgct
His Ile Pro Ser Pro
                                                                       471
geggtgaage tttcccattt tatgtgcaga ttattttcag agggtatata gaattcagge
                                                                       526
agetgttteg ttgtageaca ttaaaaatat ttteecaett caaaaaaaaa aaace
```

```
<210> 320
<211> 989
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 44..814
<221> sig_peptide
<222> 44..112
<223> Von Heijne matrix
      score 8.30000019073486
      seq VRLLLXLLLLIA/LE
<221> polyA_site
<222> 978..989
<400> 320
aaatgtgtac acgcccagct tcctgcctgt tactctccac agt atg cga aga ata
                                                Met Arg Arg Ile
                                                                     103
tee etg act tet age eet gtg ege ett ett ttg tdt etg etg ttg eta
Ser Leu Thr Ser Ser Pro Val Arg Leu Leu Leu Xaa Leu Leu Leu Leu
                -15
                                    -10
                                                                     151
cta ata gcc ttg gag atc atg gtt ggt ggt cac tct ctt tgc ttc aac
Leu Ile Ala Leu Glu Ile Met Val Gly Gly His Ser Leu Cys Phe Asn
                                                                     199
ttc act ata aaa tca ttg tcc aga cct gga cag ccc tgg tgt gaa gcg
Phe Thr Ile Lys Ser Leu Ser Arg Pro Gly Gln Pro Trp Cys Glu Ala
                       20
                                                                     247
cat gtc ttc ttg aat aaa aat ctt ttc ctt cag tac aac agt gac aac
His Val Phe Leu Asn Lys Asn Leu Phe Leu Gln Tyr Asn Ser Asp Asn
                    35
                                        40
aac atg gtc aaa cct ctg ggc ctc ctg ggg aag aag gta tat gcc acc
                                                                      295
Asn Met Val Lys Pro Leu Gly Leu Leu Gly Lys Lys Val Tyr Ala Thr
                                    55
age act tgg gga gaa ttg ace caa acg etg gga gaa gtg ggg ega gae
Ser Thr Trp Gly Glu Leu Thr Gln Thr Leu Gly Glu Val Gly Arg Asp
            65
                                70
ctc agg atg ctc ctt tgt gac atc aaa ccc car ata aag acc agt gat
                                                                      391
Leu Arg Met Leu Leu Cys Asp Ile Lys Pro Gln Ile Lys Thr Ser Asp
                                                                      439
cot too act otg caa gto kar atk ttt tgt caa cgt gaa gca gaa cgg
Pro Ser Thr Leu Gln Val Xaa Xaa Phe Cys Gln Arg Glu Ala Glu Arg
                                            105
                        100
                                                                      487
tgc act ggt gca tcc tgg cag ttc gcc acc aat gga gag aaa tcc ctc
Cys Thr Gly Ala Ser Trp Gln Phe Ala Thr Asn Gly Glu Lys Ser Leu
                                        120
                    115
ctc ttt gac gca atg aac atg acc tgg aca gta att aat cat gaa gcc
                                                                      535
Leu Phe Asp Ala Met Asn Met Thr Trp Thr Val Ile Asn His Glu Ala
                                     135
                130
                                                                      583
agt wag atc aag gag aca tgg aag aaa gac aga ngg ctg gaa aak tat
Ser Xaa Ile Lys Glu Thr Trp Lys Lys Asp Arg Xaa Leu Glu Xaa Tyr
                                 150
                                                     155
            145
ttc agg aag ctc tca aar gga gac tgc gat cac tgg ctc agg gaa ttc
Phe Arg Lys Leu Ser Lys Gly Asp Cys Asp His Trp Leu Arg Glu Phe
                                                170
         160
                            165
                                                                       679
tta ggg cac tgg gaa gca atg cca raa ccg ama gtg tcm cca rta aat
```

Leu Gly His Trp Glu Ala Met Pro Xaa Pro Xaa Val Ser Pro Xaa Asn	
175 180 185 gct toa raw ato cao tgg tot tot tot art ota coa raw ara tgg ato	727
Ala Ser Xaa Ile His Trp Ser Ser Ser Xaa Leu Pro Xaa Xaa Trp Ile 190 195 200 205	
ato otg ggg gca tto ato otg tta vtt tta atg gga att gtt oto ato	775
Ile Leu Gly Ala Phe Ile Leu Leu Xaa Leu Met Gly Ile Val Leu Ile 210 215 220	
tgt gtc tgg tgg caa aat ggc ara ara tcc acc tad arg tgataccacg	824
Cys Val Trp Trp Gln Asn Gly Xaa Xaa Ser Thr Xaa Xaa 225 230	
geggegeaaa attgtteace tgtggteete gategetgae ageettgget eccaetgetg	884
tgtgttccct gagtcaagtg gaggcggagc ctgcaatgag cggaratcgc gcctctgcat tccagtcttg gcaacagarc aagactccgt ctcaaaaaaa aaaaa	944 989
tictageting geaacagare aagaceerge circaaaaaaa aaaaa	303
<210> 321	
<211> 1017	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 3581	
<221> sig_peptide	
<222> 3182	
score 6.69999980926514	
seq LWPFLTWINPALS/IC	
<221> polvA site	
<221> polyA_site <222> 10061016	
<222> 10061016	
<222> 1006. 1016 <400> 321	47
<222> 10061016  <400> 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu	47
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu   -60</pre>	-
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu   -60</pre>	<b>47</b> 95
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu   -60</pre>	95
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu   -60</pre>	-
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu   -60</pre>	95
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu   -60</pre>	95
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu   -60</pre>	95 143
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191 239
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg     Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287
<pre>&lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287 335

70 75 80	
ttc cas aaa cat ctg ttg gtg ctg ctg gtg gct gtg gcc cat agt gtt Phe Xaa Lys His Leu Leu Val Leu Leu Val Ala Val Ala His Ser Val	479
ctg gaa cca cct gcc ctg gtc cca aat gtg cag tgt gag atg tgc aca Leu Glu Pro Pro Ala Leu Val Pro Asn Val Gln Cys Glu Met Cys Thr	527
100 105 110 115 cac tca ggg ccc cgt gac ctg gaa gcc gca gtc gtg tcc cca gca cct His Ser Gly Pro Arg Asp Leu Glu Ala Ala Val Val Ser Pro Ala Pro	575
120 125 130 tgg gaa tgagcctgtc ctctgtgtga aggagggggt ggttctcaaa ccactgactc	631
Trp Glu  ttggtgctca ggaggggcct gctgctgtcc tgggcatggg gtggtcattg ttcaagactg aggcagactc agtctttgaa agggtgcaga ggccaggcgc ggtggctcac gcctgtaatt ccagcacttt gggaggccaa ggtggacaga tcatgaggtc aggagttcga gaccagcctg gccaatacgg tgaaaccgca tctctactaa rraatawcaw aaattagtcg ggcatgggtg atgtgtgctt gtagtcccag ctactcatga ggyctgaggc agaagaatca cctgaatctg ggaggcagag gttgcagtga accaagatcg cacgactgta caccagcctg ggcgacagag tgagactccg tctcaaaaaa aaaaam	691 751 811 871 931 991
<210 > 322 <211 > 529 <212 > DNA <213 > Homo sapiens	·
<220> <221> CDS <222> 107427	
<221> sig_peptide <222> 107190 <223> Von Heijne matrix score 3.79999995231628 seq RFLSLSAADGSDG/SH	
<221> polyA_signal <222> 499504	
<221> polyA_site <222> 516529	
<400> 322 aaagtcagcg ctggagtcgg ctaggcggct ggaaacggcg gctgccgccg gtgactcagg gaggcgggag gccgmsggmg gagctcttcc tgcaggcgtg garacc atg gtg ctc	60 115
Met Val Leu  acg ctc gga gaa agt tgg ccg gta ttg gtg ggg agg agg ttt ctc agt  Thr Leu Gly Glu Ser Trp Pro Val Leu Val Gly Arg Arg Phe Leu Ser  -20  -15  -10	163
-25 ctg tcc gca gcc gac ggc agc gat ggc agc cac gac agc tgg gac gtg Leu Ser Ala Ala Asp Gly Ser Asp Gly Ser His Asp Ser Trp Asp Val -5	211
gag cgc gtc gcc gag tgg ccc tgg ctc tcc ggg acc att cga gct gtt Glu Arg Val Ala Glu Trp Pro Trp Leu Ser Gly Thr Ile Arg Ala Val 10 15 20	259
tcc cac acc gac gtt acc aag aag gat ctg aag gtg tgt gtg gaa ttt Ser His Thr Asp Val Thr Lys Lys Asp Leu Lys Val Cys Val Glu Phe 25 30 35	307
gak ggg gaa tot tgg agg aaa aga aga tgg ata gaa gto tac ago ott Xaa Gly Glu Ser Trp Arg Lys Arg Arg Trp Ile Glu Val Tyr Ser Leu 40 45 50 55	355

cta agg aaa gca ttt tta gta aaa cat aat ttg gtt tta gct gaa cga Leu Arg Lys Ala Phe Leu Val Lys His Asn Leu Val Leu Ala Glu Arg 60 65 70	403
aag toa oot gaa att tot tgg ggt taaccatott tagttaaatg gaattttaat Lys Ser Pro Glu Ile Ser Trp Gly	457
ttaaatgacg ctttgctaat tttaagtgtt aagcattttg cattaaaata ttcatataat aaaaaaaaa aa	517 529
<210> 323 <211> 1046	
<211> 1046 <212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS <222> 45407	
<222> 45407	
<221> sig_peptide	
<222> 4583	
score 5.69999980926514	
seq MLVLRSALTRALA/SR	
<221> polyA_signal <222> 10081013	
<221> polyA_site	
<222> 10321042	
<400> 323	56
aaaaggacac ggctggctgc ttttctcagc gccgaagccg cgcc atg ctc gtc ctc Met Leu Val Leu	36
-10	104
aga agc gcc ctg act cgg gcg ctg gcc tca cgg acg ctg gcg cct cag Arg Ser Ala Leu Thr Arg Ala Leu Ala Ser Arg Thr Leu Ala Pro Gln	104
-5 1 5	
atg tgc tca tct ttt gct acg gga ccc aga caa tac gat gga ata ttc Met Cys Ser Ser Phe Ala Thr Gly Pro Arg Gln Tyr Asp Gly Ile Phe	152
10 15 20	
tat gaa tit ogt tot tat tac ott aag ooc toa aag atg aat gag tio	200
Tyr Glu Phe Arg Ser Tyr Tyr Leu Lys Pro Ser Lys Met Asn Glu Phe 25 30 35	
	248
ctg gaa aat ttt gag aaa aac gct caa ctt cgg aca gct cac tct gaa	
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu	
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu 40 45 50 55	296
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu  40 45 50 55  ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg  Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val	296
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu 40 45 50 55  ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val 60 65 70	296 - 344
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu 40 45 50 55  ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val 60 65 70  ttt cat att tgg aag tat gat aat ttt gct cat cga act gaa ttt cag	-
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu 40 45 50 55  ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg  Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val 60 65 70  ttt cat att tgg aag tat gat aat ttt gct cat cga act gaa ttt cag  Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg Thr Glu Phe Gln 75 80 85	344
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu 40 45 50 55  ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg  Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val 60 65 70  ttt cat att tgg aag tat gat aat ttt gct cat cga act gaa ttt cag  Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg Thr Glu Phe Gln 75 80 85  aaa gcc ttg gcc aaa gat aag gaa tgg caa gaa caa ttc ctc att cca	-
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu 40 45 50 55  ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val 60 65 70  ttt cat att tgg aag tat gat aat ttt gct cat cga act gaa ttt cag Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg Thr Glu Phe Gln 75 80 85  aaa gcc ttg gcc aaa gat aag gaa tgg caa gaa caa ttc ctc att cca Lys Ala Leu Ala Lys Asp Lys Glu Trp Gln Glu Gln Phe Leu Ile Pro 90 95 100	344 392
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu 40 45 50 55  ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val 60 65 65 65 67  ttt cat att tgg aag tat gat aat ttt gct cat cga act gaa ttt cag Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg Thr Glu Phe Gln 75 80 85  aaa gcc ttg gcc aaa gat aag gaa tgg caa gaa caa ttc ctc att cca Lys Ala Leu Ala Lys Asp Lys Glu Trp Gln Glu Gln Phe Leu Ile Pro 90 95 100 aat ttg gct ctc aat tgataaacaa gatagtgaga ttacttatct ggtaccatgg	344
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu 40 45 50 55  ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val 60 65 65 65 66 67 68 68 68 68 68 68 68 68 68 68 68 68 68	344 392
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu 40 45 50 55  ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val 60 65 65 65 67  ttt cat att tgg aag tat gat aat ttt gct cat cga act gaa ttt cag Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg Thr Glu Phe Gln 75 80 85  aaa gcc ttg gcc aaa gat aag gaa tgg caa gaa caa ttc ctc att cca Lys Ala Leu Ala Lys Asp Lys Glu Trp Gln Glu Gln Phe Leu Ile Pro 90 95 100 aat ttg gct ctc aat tgataaacaa gatagtgaga ttacttatct ggtaccatgg	344 392

627

747

ctaggctaca caaaactagt tggagtgttc cacacagagt acggagcact caacagagtt

catgttottt ggtggaatga gagtgcagat agtogtgcag otgggagaca taagtoocat gaggatooca gagttgtggc agotgttogg gaaagtgtoa actaootagt atotoagoag

```
aatatgette tgatteetae ategttttea eeactgaaat agttttetae tgaaatacaa
                                                                     807
aacatttcat taactgctat aggatctgtc tgctaatggt gcttaaattc tcccaagagg
                                                                     867
ttctcacttt tatttgaagg aggtggtaag ttaatttgct atgtttcttg cattatgaag
                                                                     927
gctacatctg tgctttgtaa gtaccacttc aaaaaatakt tctgtttact ttctgcatgg
                                                                     987
tatttcagtg tctgtcatac attaaaaata cttgtcactg tttyaaaaaa aaaaammcc
                                                                    1046
<210> 324
<211> 880
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 201..332
<221> sig_peptide
<222> 201..251
<223> Von Heijne matrix
      score 7.80000019073486
      seq VLWLISFFTFTDG/HG
<221> polyA site
<222> 869..880
<400> 324
aattgctgat ggatcagtga gcctgtgttc atgccagtga gctgctgtgg ctcagatact
                                                                      60
gatacttict ticcaaacag cataagaagt gattgancca caagtatact gaaggmargg
                                                                     120
yhocowswar tyctggwgtg amgagataaa toaccagtoa cagactatgo accegactgo
                                                                     180
tgctgttcag tccagggaaa atg aaa gtt gga gtg ctg tgg ctc att tct ttc
                                                                     233
                      Met Lys Val Gly Val Leu Trp Leu Ile Ser Phe
                              -15
                                                  -10
                                                                     281
ttc acc ttc act gac ggc cac ggt ggc ttc ctg ggg gtg agt tgg tgc
Phe Thr Phe Thr Asp Gly His Gly Gly Phe Leu Gly Val Ser Trp Cys
tat gto toa tat etc tto tea act aac tot eet etc teg tto egg ege
                                                                      329
Tyr Val Ser Tyr Leu Phe Ser Thr Asn Ser Pro Leu Ser Phe Arg Arg
                15
                                 20 .
                                                                      382
att tagaacccct cactctctag gggactgcaa ctgcataatt taatgtactt
                                                                      442
gagatcagaa gtcctgagtt ctcgtttcaa cattaccaac attcactgtg tggccttgga
taaqtraqtc atttcatctc ttcqqaqctt agatqatcma actqcaarag gaggatcttt
                                                                      502
                                                                      562
gattamacta tottaqaqat cttttccagt tcaacacatg ctgtactatg gcttctcgga
                                                                      622
tgcagaaaaa tcacatggat ggacattagc aatcettara cactgtettt cetgtetaca
                                                                      682
ctcgcttgag tgatgckttc atctaggatc atggttttaa tattctctac atgctgatga
                                                                      742
ctcccagctg tatagctcca tctcagaacc tctcccctgt ccacactcac atatccatta
                                                                      802
cctacgtgtt atttccagct gggaaatcca gcggaacctc ggnaacttca tttgnttcaa
aatcgnaacc caatcettet tgeetatete ageaagtggt atcactatet ttecagetac
                                                                      862
                                                                      880
ttaggcaaaa aaaaaaaa
```

<210> 325

<211> 1217

<212> DNA

<213 > Homo sapiens

```
<221> CDS
<222> 217..543
<221> sig_peptide
<222> 217..255
<223> Von Heijne matrix
      score 6.40000009536743
      seq MCLLTALVTQVIS/LR
<221> polyA_site
<222> 1206..1217
<400> 325
                                                                      60
aatgccagtg tcagcttctc tccgaaaact gggtaatacg aaatggtctt tattggttgt
gaacactcga gctgagaaac attttaggat ctttgtgtct tttgtgatga ttttgtttct
                                                                     120
                                                                     180
graagrwgga aasctgtcta aaaatattca agtgtgcaac caaggattta gatgaagcca
qcaaacaaaq gaatcatgta atcaggacct gagcga atg tgc tta ctc acg gcg
                                                                     234
                                        Met Cys Leu Leu Thr Ala
                                                                     282
tta gtt aca cag gtg att tcc tta aga aaa aat gca gag aga act tgt
Leu Val Thr Gln Val Ile Ser Leu Arg Lys Asn Ala Glu Arg Thr Cys
        - 5
tta tgc aag agg aga tgg ccc tgg ngc ccc tcg ccc cgg atc tac tgc
                                                                     330
Leu Cys Lys Arg Arg Trp Pro Trp Xaa Pro Ser Pro Arg Ile Tyr Cys
                                        20
                   15
                                                                     378
tca tcc acc cca tgc gat tcc aaa ttc ccc acc gtc tac tcc agt gcc
Ser Ser Thr Pro Cys Asp Ser Lys Phe Pro Thr Val Tyr Ser Ser Ala
                                    35
               30
cca ttc cat gcc ccc ctc ccc gtc cag aat tcc tta tgg ggg cac ccg
                                                                     426
Pro Phe His Ala Pro Leu Pro Val Gln Asn Ser Leu Trp Gly His Pro
                                50
           45
ctc cat ggt tgt tcc tgg caa tgc cac cat ccc cag gga car aat ctc
                                                                      474
Leu His Gly Cys Ser Trp Gln Cys His His Pro Gln Gly Gln Asn Leu
                                                70
                            65
                                                                      522
cag cct gcc agt ctc cad acc cat ctc tcc aag ccc aag cgc cat ttt
Gln Pro Ala Ser Leu Xaa Thr His Leu Ser Lys Pro Lys Arg His Phe
                        80
    75
ara aar aar rra tgt caa gcc tgatgaarac atgagtggca aaaacattgc
                                                                      573
Xaa Lys Lys Xaa Cys Gln Ala
aatgtacara aatgagggtt totatgotga toottacott tatcacgagg gacggatgag
catascetea teccatggtg gacacecaet ggatgteece gaccacatea ttgcatatea
ccgcaccgcc atccggtcag cgagtgctta ttgtaacccc tcaatgcaag cggaaatgca
                                                                      753
tatggaacaa tcactgtaca gacagaaatc aaggaaatat ccggatagcc atttgcctac
                                                                      813
actgggctcc aaaacacccc ctgcctctcc tcacagaktc agtgacctga ggatgataga
                                                                      873
                                                                      933
catgcacgct cactataatg cocacggccc coctcacacc atgcagccag accgggcctc
                                                                      993
tecgageege caggeettta aaaaggagee aggeacettg gtgtatatag aaaageeacg
gagegetgea ggattateca geettgtaga eeteggeeet eetetaatgg agaageaagt
                                                                     1053
                                                                     1113
ttttgcctac agcacggcga caatacccaa agacagagag accagagaga ggatgcaagc
catggagaaa cagattgcca gtttaactgg ccttgttcag tctgcgcttt ttaaagggcc
                                                                     1173
                                                                     1217
cattacaagt tatagcaaar atgcgtctag ctaaaaaaaa aaaa
```

<210> 326

<211> 959

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 18..446

```
<221> sig_peptide
  <222> 18..140
  <223> Von Heijne matrix
       score 4.09999990463257
        seq GILILWIIRLLFS/KT
 <221> polyA signal
 <222> 930..935
 <221> polyA_site
 <222> 948..959
 <400> 326
 aaaggaageg getaaet atg geg ace gee acg gag cag tgg gtt etg gtg
                                                                      50
                    Met Ala Thr Ala Thr Glu Gln Trp Val Leu Val
                                           -35
 gag atg gta cag gcg ctt tac gag gct cct gct tac cat ctt att ttg
                                                                      98
 Glu Met Val Gln Ala Leu Tyr Glu Ala Pro Ala Tyr His Leu Ile Leu
 - 30
                    -25
                                        -20
 gaa ggg att ctg atc ctc tgg ata atc aga ctt ctt ttc tct aag act
                                                                    146
Glu Gly Ile Leu Ile Leu Trp Ile Ile Arg Leu Leu Phe Ser Lys Thr
                -10
                                    -5
 tac aaa tta caa gaa cga tct gat ctt aca gtc aag gaa aaa gaa gaa
                                                                    194
Tyr Lys Leu Gln Glu Arg Ser Asp Leu Thr Val Lys Glu Lys Glu Glu
                           10
ctg att gaa gag tgg caa cca gaa cct ctt gtt cct cct gtc cca aaa
                                                                    242
Leu Ile Glu Glu Trp Gln Pro Glu Pro Leu Val Pro Pro Val Pro Lys
                        25
                                           30
gac cat cct gct ctc aac tac aac atc gtt tca ggc cct cca agc cac
                                                                    290
Asp His Pro Ala Leu Asn Tyr Asn Ile Val Ser Gly Pro Pro Ser His
                    40.
                                        45
aaa act gtg gtg aat gga aaa gaa tgt ata aac ttc gcc tca ttt aat
                                                                    338
Lys Thr Val Val Asn Gly Lys Glu Cys Ile Asn Phe Ala Ser Phe Asn
                55
                                   60
ttt ctt gga ttg ttg gat aac cct agg gtt aag gca gca gct tta gca
                                                                    386
Phe Leu Gly Leu Leu Asp Asn Pro Arg Val Lys Ala Ala Ala Leu Ala
                                75
tot ota aag aag tat ggc gtg ggg act tgt gga coo tgt gga ttt tat
                                                                    434
Ser Leu Lys Lys Tyr Gly Val Gly Thr Cys Gly Pro Cys Gly Phe Tyr
                            90
ggc aca ttt gaa tgaaratgaa ggatcattga tttccttgtg tatggataat
                                                                    486
Gly Thr Phe Glu
    100
ccgggaacag gccaactaaa tatttgatga atgtatgatt tcaaatacag tgaattccct
                                                                    546
gggagtcatc aaaraagacg gcattttatg gttgttttta ttaagtgtat attctttgct
                                                                    606
cctgaaaatg ttattaaata attgtttagg ccgggcatgg tggctcatgc ctgtaatccc
                                                                    666
ageaetttea aaggetgagg caggeagate acetgaggte aggagtteaa aaceageetg
gccaacatgc tgaaacctcg tctctactaa aaatacaaaa attagctggg cgtggtggtg
                                                                    786
grtgcctgtg gtcccagetr cgtgggaggc tgaggtggga gaattgcttc aacctgggag
                                                                    846
geggaggttg cagtgageeg agateatgee actgeactee ageetgggea acagageaag
                                                                    906
959
```

<210> 327 <211> 921 <212> DNA

<213> Homo sapiens

<220>

<221> CDS

WO 99/31236 -244 - PCT/IB98/02122

<222> 29..724 <221> sig_peptide <222> 29..118 <223 > Von Heijne matrix score 3.90000009536743 seg VAHALSLPAESYG/NX <221> polyA signal <222> 886..891 <221> polyA site <222> 910..920 <400> 327 aaggagccac gctttcgggg gttgcaag atg gcg gcc acc agt gga act gat 52 Met Ala Ala Thr Ser Gly Thr Asp -30 -25 gag ccg gtt tcc ggg gag ttg gtg tct gtg gca cat gcg ctt tct ctc 100 Glu Pro Val Ser Gly Glu Leu Val Ser Val Ala His Ala Leu Ser Leu -15 -10 -20 cca gca gag tcg tat ggy aac grt yct gac att gag atg gct tgg gcc 148 Pro Ala Glu Ser Tyr Gly Asn Xaa Xaa Asp Ile Glu Met Ala Trp Ala 1 atg aga gca atg cag cat gct gaa gtc tat tac aag ctg att tca tca 196 Met Arg Ala Met Gln His Ala Glu Val Tyr Tyr Lys Leu Ile Ser Ser 15 20 gtt gac cca cag ttc ctg aaa ctc acc aaa gta gat gac caa att tac 244 Val Asp Pro Gln Phe Leu Lys Leu Thr Lys Val Asp Asp Gln Ile Tyr 35 30 tct gag ttc cgg aaa aat ttt gag acc ctt agg ata gat gtg ttg grc 292 Ser Glu Phe Arg Lys Asn Phe Glu Thr Leu Arg Ile Asp Val Leu Xaa 50 55 cca gaa gan ctc aag tca gaa tca gcn aaa gag ccc cca gga tac aat 340 Pro Glu Xaa Leu Lys Ser Glu Ser Ala Lys Glu Pro Pro Gly Tyr Asn 65 388 tot ttg cca ttg aaa ttg ctc gga acc ggg aag gct ata aca aag ctg Ser Leu Pro Leu Lys Leu Leu Gly Thr Gly Lys Ala Ile Thr Lys Leu 80 85 436 ttt ata tca gtg ttc agg aca aag aag gag aga aag gag tca aca atg Phe Ile Ser Val Phe Arg Thr Lys Lys Glu Arg Lys Glu Ser Thr Met 100 95 gag gag aaa aaa gag ctg aca gtg gag aag aag aga aca cca aga atg Glu Glu Lys Lys Glu Leu Thr Val Glu Lys Lys Arg Thr Pro Arg Met 115 110 gag gag aga aag gag ctg ata gtg gag aag aaa aag agg aag gaa tca 532 Glu Glu Arg Lys Glu Leu Ile Val Glu Lys Lys Lys Arg Lys Glu Ser 130 580 aca gag aag aca aaa ctg aca aag gag gag aaa aag gga aag aag ctg Thr Glu Lys Thr Lys Leu Thr Lys Glu Glu Lys Lys Gly Lys Leu 145 150 628 aca aag aaa tca aca aaa gtg gtg aaa aag cta tgt aag gta tac agg Thr Lys Lys Ser Thr Lys Val Val Lys Lys Leu Cys Lys Val Tyr Arg 165 160 gaa cag cac tot aga ago tat gao toa att gag act aca agt acc acg 676

gtg cta ctt gca cag acc cct ttg gtt aaa tgt aaa ttc ttg tac aat 724
Val Leu Leu Ala Gln Thr Pro Leu Val Lys Cys Lys Phe Leu Tyr Asn
190 195 200
tgaaggatac gcagaaggac atcttctag tctaacagtc aggagctgct ctggtcattc
ccttgtatga actggtctaa agactgttag tggggtgtta gttgatttt cctggtatac 844

Glu Gln His Ser Arg Ser Tyr Asp Ser Ile Glu Thr Thr Ser Thr Thr

921

tgtttcttgg ctgacactac tggtcaagta agaaatttgt aaataaattt cttttggttc

ttattaamaa aaaaaas

<210> 328 <211> 1344 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 404..586 <221> sig_peptide <222> 404..466 <223> Von Heijne matrix score 4.09999990463257 seq SLMFFSMMATCTS/NV <221> polyA signal <222> 1304..1309 <221> polyA_site <222> 1334..1344 <400> 328 ataatttaat gcaaaatatc cttttatgaa tttcatgtta atattgtgaa atattaaaat aattccacaa tagttgagaa aaatgagcat ttttttccat ttttaaaaaa tgcatagaaa 120 agacaatttt aaaatcctgg gamccawatt tatttagaag tagctgttag taaaacatta 180 gaaaaggagt caggccatba ggttatttat nbnaatctct aagcaattag gntgaagtta 240 300 ttaaqtcaaq cctaqaaaaq ctqcctcctt gtaaggcttt catgacaatg tatagtaatc 360 breagtgtee aattettege acteeteagg aatateacta ceteaggtta eggtacacag 415 gctataattg atgatgatgt tcagataact gaagacacaa taa atg aca ttc aga Met Thr Phe Arg 463 cat cag gac aat too oto atg tto ttt tot atg atg goo acc tgt acc His Gln Asp Asn Ser Leu Met Phe Phe Ser Met Met Ala Thr Cys Thr - 15 -10 511 ago aac gtg ggt tto acc cac aca acg atg aac tgt tot ott act tot Ser Asn Val Gly Phe Thr His Thr Thr Met Asn Cys Ser Leu Thr Ser 10 559 cca gtt gat ttt aaa gac ttg tta aga gtc tta cta ata aaa ttt ggg Pro Val Asp Phe Lys Asp Leu Leu Arg Val Leu Leu Ile Lys Phe Gly 25 606 tat gat aga aaa too aca ato aaa tot tgaaccaaat aacatattaa Tyr Asp Arg Lys Ser Thr Ile Lys Ser 35 40 attactaata titaagtgat ggaagacaca caaaaaactt aaaagcacga acaacctaac 666 726 ttgaaaaara attttaaaat atgattaacc tgaaraaaar araatcctaa ragccaaagc 786 tectttttat ttagettgga atttteetat tggtteetaa caaactgtee caatgteata 846 taaggaaaca tgatctatta cattccttta taacaacgtg gararactat aaacctatgt aagtagtaaa actatatcag adactcagga ractgactww aaggcctgga tctgcagtgt 906 attatctgta taaaaattgg cagggggaag ctaaaaggaa aggagattgg agatctcaat totatcatgg tgtatttcat acgcaaatca ragcatgcat tgttttttgt ttttggaaar 1026 avaarggaag tgtgttctgc cccatgtttc cttccgtgtt tatagttcaa actctatata 1086 tacttcaggt attttttgtt tagcccttca ttataaatgg gcaggaaatt gtttatcaac 1146 ctagccagtt tattactagt gaccttgact tcagtatett gagcattett ttatattttt 1206 cttttattat cctgagtctg taactaaaca attttgtctt caaattttta tccaatatcc 1266 attgcaccac accaaatcaa gcttcttgat tttcaaaaat aaaaaggggg aaatacttac 1326 1344 aacttgtaaa aaaaaaaa

```
<210> 329
 <211> 585
 <212> DNA
 <213> Homo sapiens
<220>
<221> CDS
<222> 331..432
 <221> sig_peptide
 <222> 331..387
 <223> Von Heijne matrix
       score 7
       seq AGLSSCLLPLCWL/ER
 <221> polyA_signal
 <222> 548..553
 <221> polyA_site
 <222> 573..585
 <400> 329
aagcctaggt gtggcgcccc gaccggactt tcacttctgg ccagcccttt ccccacctgg
gcgcgggass ggtgccagtc tttaaacaac ctctcgatgg gtcccacgaa gatgtttcca
                                                                       120
gaccettgga atgecaagtt caagtttage tatgtetege ggagaggeeg gtggaagaag
                                                                       180
                                                                       240
caacgagaat gaagcaccóc agttctctgc tgagcacatg ggcatctgca ataaagattt
aatttcccag cttctcctga agctcggtat ggccacaaca ctaaattctg cccgaggaga
                                                                       300
ttgagcaaaa tagtatggga cttccaagaa atg ttt tta aag tca ggg gca ggc
                                                                       354
                                  Met Phe Leu Lys Ser Gly Ala Gly
                                                                       402
 ctt tot toa tgo ott ott oot ott tgo tgg otg gaa ogo aaa gac oat
 Leu Ser Ser Cys Leu Leu Pro Leu Cys Trp Leu Glu Arg Lys Asp His
     -10
                         -5
 ggc agg agg cca agc asc cat cct gga agg tgaaagcctc atactaagga
                                                                       452
 Gly Arg Arg Pro Ser Xaa His Pro Gly Arg
                 10
                                                                       512
 cgtcaracag cgaaataara rcctgggtcc ttgaccctgt aaasatctcc ctccccatcc
                                                                       572
 tggtctgtct gccttgactc ctttcatatg aaaaaaataa acttttaact tgcgtwaacc
                                                                       585
 aaaaaaaaa aaa
 <210> 330
 <211> 914
 <212> DNA
```

<222> 886..891

<221> polyA_site <222> 903..914

<400> 330
acaaatatca atgatgttta tgaatctagt gtgaaagtkt taatcacatc acaagget 58
atg aac rra tat gca agt cca ttc aac tgw caa ttg ard tat ttg gak 106
Met Asn Xaa Tyr Ala Ser Pro Phe Asn Xaa Gln Leu Xaa Tyr Leu Xaa -50 -45 -40
• •
ttg agc agr ttc gag tgt gtr cat aga gat gga aga gta att aca ctg 154 Leu Ser Arg Phe Glu Cys Val His Arg Asp Gly Arg Val Ile Thr Leu
-35 -30 -25
tot tat dag gag dag gag ota dag gat tit dit dig tot dag atg toa 202
Ser Tyr Gln Glu Gln Glu Leu Gln Asp Phe Leu Leu Ser Gln Met Ser
-20 -15 -10
cag cac cag gta cat gca gtt cag caa ctc gcc aag gtt atg ggc tgg 250
Gln His Gln Val His Ala Val Gln Gln Leu Ala Lys Val Met Gly Trp
-5 1 5 10
caa gta ctg agc ttc agt aat cat gtg gga ctt gga cct ata gag agc 298
Gln Val Leu Ser Phe Ser Asn His Val Gly Leu Gly Pro Ile Glu Ser
15 20 25
abt ggt aat gca tot gcc atc acg gtg gcc ccc caa gtg gtg act atg 346
Xaa Gly Asn Ala Ser Ala Ile Thr Val Ala Pro Gln Val Val Thr Met
30 35 40
cta ttt cag ttc gta atg gac ctg aaa gtg gca gca aga tta tgg ttc 394
Leu Phe Gln Phe Val Met Asp Leu Lys Val Ala Ala Arg Leu Trp Phe
45 50 55  agr fro ofe gra acc aat gra aar acc tto caa aaa grg atg ttt tac 442
agt ttc ctc gta acc aat gta aar acc ttc caa aaa gtg atg ttt tac 442 Ser Phe Leu Val Thr Asn Val Lys Thr Phe Gln Lys Val Met Phe Tyr
60 65 70
aar ata aca aat gga gtc atc ttc gtg tgc cat tca aar aag ttc agt 490
Lys Ile Thr Asn Gly Val Ile Phe Val Gly His Ser Lys Lys Phe Ser
75 80 85 90
gga ata aaa tgg aag gtc kaa att ttg ttt ata aaa tgg arm tgc tta 538
Gly Ile Lys Trp Lys Val Xaa Ile Leu Phe Ile Lys Trp Xaa Cys Leu
95 100 105
tgt ctg cac tta gcc ctt gtc tac tat gat ttt ttc car atg ttt cct 586
Cys Leu His Leu Ala Leu Val Tyr Tyr Asp Phe Phe Gln Met Phe Pro
110 115 120
aaa raa gtt tcc ara aac ttt gac ttg aaa tgt ttg car atc aac tat 634
Lys Xaa Val Ser Xaa Asn Phe Asp Leu Lys Cys Leu Gln Ile Asn Tyr
125 130 135
aag cac aaa gaa gar ata act tcc aaa aga gtg ctg ttt tta aaa ata 682
Lys His Lys Glu Glu Ile Thr Ser Lys Arg Val Leu Phe Leu Lys Ile
140 145 150 are arr agg as a ror fit att taggagette asacettega ettetatasat 733
ata att agg ada tgt tot att tagenteet annetteet and
Ile Ile Arg Lys Cys Phe Ile
155 160 assaurant transport of the same of
decadeder reduced adaptered and along the control and along the co
aaaataatat gtttttcatg cagtttaaaa tattactaac ttaagggttt ctatgtgctt 853 tttaaaatat tccttctttg atgttgacat caaataaagt atgtggttta aaaaaaaaaa
914

<210> 331

<211> 1161

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 672..752

```
<221> sig_peptide
<222> 672..722
<223> Von Heijne matrix
      score 4.30000019073486
      seq LLYAHLSFTSKRA/VV
<221> polyA_site
<222> 1150..1161
<400> 331
                                                                      60
aagatatcac tqtcttqttt tcacttagat cctacttaca aagtgagggt tattaacaga
ataaagcett cetttaaage tttataataa teatatttat taataatget gttgtgcata
                                                                     120
                                                                     180
cttatagtat gcatatattc agcatatgtt gcatgtsttc agaattacat aagatgaaat
                                                                     240
ccctttcatt gcaacttgca agtgagaaaa gatccttagt ggctctggtg gaagaaatag
                                                                     300
tatttettet teteagggtg tetecetgee ttggeceete ceagaageee eggetttaaa
                                                                     360
agtgaaaatg tttgaaacat gaaacatgtc tgtaggaagc atcagcatgg ccataagtgc
artgattttc atatatgcct ctgcccattt caaatatatt tttgacatga ataaatctaa
                                                                     420
cagtatacar aataattcat gtaaraccct aacgtgtaca tgtgaaaaag catttctata
                                                                     480
taatgtgagg agcactggcc atcaattagg gaaataaagg tcatgtaata ttgcaaattt
                                                                     540
tcaaaataga gcsstgcaag ataactgcaa tcataccaaa aactatttga gtaaatggat
ttttaaagta atttttgttt aaaaaaattt atatttcaga agsagaaaat gtcaaatgat
                                                                     660
agtotttgta a atg gtg gtg cac ott oto tat gca cat otg tot ttt aca
                                                                     710
             Met Val Val His Leu Leu Tyr Ala His Leu Ser Phe Thr
                                         -10
                     -15
                                                                     752
tca aaa aga gct gtg gtc atg cta aaa tta gag ata act ttt
Ser Lys Arg Ala Val Val Met Leu Lys Leu Glu Ile Thr Phe
                1
tgaatgactt ggtcaagctg tgtgtaaaat atttaaccat aagtcaagta cagtgtacta
                                                                     812
                                                                     872
tgtttaataa agttacattt aatgcattta ttgcatatat gaatatatac atgaagaggc
                                                                     932
tttatgtctt ctggtatttg attttgaatg ttttttaagt cagtggtgcc tttaggcaag
aactttcgaa attaatcatt ctttgtgttt tctgattttt caggtaacat gtacactatt
                                                                     992
tagaaaccat catagtttat tcaccttaaa aaattgattg tattatttaa atatatcact
                                                                    1052
tagatgggca tttcctataa ttaggatatt ccaaatagtt gctgaaatca attgtgccat 1112
                                                                    1161
tgaccaatgg atgcacttgg ttagccttaa ttttttyaaa aaaaaaaaa
<210> 332
<211> 363
<212> DNA
<213> Homo sapiens
<221> CDS
<222> 57..311
<221> sig_peptide
<222> 57..128
<223> Von Heijne matrix
      score 5.30000019073486
      seq LFHLLFLPHYIET/FK
<221> polyA_signal
<222> 332..337
<221> polyA_site
<222> 351..363
<400> 332
acatttetta etgeettaeg etcateetga ggtecaeett ggtetetaaa aacaee atg
```

-			_		atg Met					_			_			107
					gaa Glu			_		_	•			_		155
			_	-	ttc Phe 15	-							_			203
					tct Ser											251
					ttc Phe											299
	gac Asp			tgat	tact	ca t	tata	atcc	tc aa	ataaa	atati	tg:	ttga	acca		351
aaaa	aaaa		aa													363
<211 <212	)> 33 L> 64 2> DN	5 IA	sapie	ens												
	)> L> CI 2> 80		32													
<222		on He core	27 ⊇ijne 3.70	e mai	erix 00476 LSRA,		2									
	l> po l> 6:		_	naļ												
	l> po 2> 63		-	ę												
acci		gt t			t at	g ct	a ag u Ar	g at	a gc	c ct	t ac	a ct	c at	c cc	ctcagc a tct o Ser	60 112
				Ala		ggt	tgg				aag	gag			cag	160
cag	ttt Phe	tct Ser	tac Tyr 15	ctt	tgc	ctg Leu	ccc	tgc Cys	ctt Leu	tca Ser	tgg Trp	aat Asr	aar Lys 25	aaa Lys	ggc Gly	208
			cag		cca Pro			tga	araa	act	aato	tcai		ggca	igttaa	262
acrt	caaa		ttac	caaa	ta r	ttat		t tt	acct	aakr	tto	acta	accc	ggti	tcaattg	322
ctt	ttta	ttt '	ttaa	tato	tt a	acto	ttca	ir ac	ittee	tacc	tca:	aaa	raac	aat	garaaca	382
ttt	gett	tac	tttc	tact	ga a	tccc	taat	c to	aaca	atct	ata	cct	ggac	tgt	cagttc	442
tcc	tcct	gta	ctat	cttc	tc t	tcta	tcca	a gt	araa	itgta	ygo	cago	garc	tcc	ttccctc	502
															actgtat	562

ttattaattt g			tttggtago	t ctggctgtgc	tatcaataaa	622 645
<210> 334 <211> 400 <212> DNA <213> Homo s	apiens					
<220> <221> CDS <222> 9129	1					
	9	231628			·	
<221> polyA_ <222> 3673	-					
<221> polyA_ <222> 3894						
<400> 334 aacaaaagga g taaaaatattt t			atg acc o		tg cct cac	60 114
ggt gga aaa Gly Gly Lys		l Leu Gly	Asp Tyr Se	t ttg gca gt		162
ccc ctg cac Pro Leu His	ttt tct ga Phe Ser As -15	t cta att p Leu Ile	tct gtt tt Ser Val Le	ta tac ctt at eu Tyr Leu Il	a ccc aaa e Pro Lys -5	210
aca ctt act Thr Leu Thr	acc aac ac Thr Asn Th	a gct gtt ir Ala Val 5	aaa cat to Lys His So	ct ata caa aa er Ile Gln Ly 10	aa aat tgt /s Asn Cys	258
atg mat ctg Met Xaa Leu 15					a agaaaaaaga	311
		cttttcatca	tatgcacc	aa atgtaaatti	tgtacaataa	371 400
<210> 335 <211> 496 <212> DNA <213> Homo s	apiens					
<220> <221> CDS <222> 1963	84			·		
<221> sig_pe						

<223> Von Heijne matrix

score 6.69999980926514 seq ILSTVTALTFARA/LD

<221> polyA_signal	
<221> polyA_site <222> 485496	
<400> 335 aaaaaattgg tcccagtttt caccctgccg cagggctggc tggggagggc agcggtttag attagccgtg gcctaggccg tttaacgggg tgacacgagc htgcagggcc gagtccaagg cccggagata ggaccaaccg tcaggaatgc gaggaatgtt tttcttcgga ctctatcgag gcacacagac agacc atg ggg att ctg tct aca gtg aca gcc tta aca ttt  Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe  -15 -10 -5	60 120 180 231
gcc aga gcc ctg gac ggc tgc aga aat ggc att gcc cac cct gca agt Ala Arg Ala Leu Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser	279
gag aag cac aga ctc gag aaa tgt agg gaa ctc gag agc agc cac tcg Glu Lys His Arg Leu Glu Lys Cys Arg Glu Leu Glu Ser Ser His Ser 15	327
gcc cca gga tca acc cag cac cga aga aaa aca acc aga aga	375
tot toa goo tgaaatgaak cogggatoaa atggttgotg atcaragooc	424
Ser Ser Ala	404
atatttaaat tggaaaagtc aaattgasca ttattaaata aagcttgttt aatatgtctc aaacaaaaaa aa	484 496
<210> 336	
<211> 968	
<212> DNA	
<213> Homo sapiens	
.220.	
<220> <221> CDS	
<222> 54590	
(222) J1J90	
<221> sig_peptide	
<222> 54227	
<223> Von Heijne matrix	
score 3.5	
seq GGILMGSFQGTIA/GQ	
<221> polyA_site <222> 955965	t
<400> 336	
atatttgccc cttactttat cttgtgcctt gagaaattgc tggggagaga ggt atg	56
Met	
tcc act ggg cag ctg tac agg atg gag gat ata ggg cgt ttc cac tcc	104
Ser Thr Gly Gln Leu Tyr Arg Met Glu Asp Ile Gly Arg Phe His Ser	
-55 -50 -45	153
cag cag cca ggt tee etc ace cca age tea ecc act gtt ggg gag att	15
Gln Gln Pro Gly Ser Leu Thr Pro Ser Ser Pro Thr Val Gly Glu Ile	
-40 -35 -30 atc tac aat aac acc aga aac aca ttg ggg tgg att ggg ggt atc ctt	20
Ile Tyr Asn Asn Thr Arg Asn Thr Leu Gly Trp Ile Gly Gly Ile Leu	
-25 -20 -15 -10	
atg ggt tot tit cag gga acc att got gga caa ggc aca gga gcc acc	24
Met Gly Ser Phe Gln Gly Thr Ile Ala Gly Gln Gly Thr Gly Ala Thr	

1

-5 1 5	
too att tot gag oto tgo aag gga caa gaa ota gag oca toa ggg got	296
Ser Ile Ser Glu Leu Cys Lys Gly Gln Glu Leu Glu Pro Ser Gly Ala 10 15 20	
ggg ctc act gtg gcc cca ccc caa gcc gtc agc ctc cag ggw atc tac	344
Gly Leu Thr Val Ala Pro Pro Gln Ala Val Ser Leu Gln Gly Ile Tyr	
25 30 35	
acc ctg cct tgg ctg cta cag ctt ttt cac tcc act gcc cta rgg gna	392
Thr Leu Pro Trp Leu Leu Gln Leu Phe His Ser Thr Ala Leu Xaa Xaa	
40 45 50 55	
dtt cag caa cet aat gga tet eta tet etg aac ate tet tea tee cat	440
Xaa Gln Gln Pro Asn Gly Ser Leu Ser Leu Asn Ile Ser Ser Ser His	
60 65 70	488
gct cor rgt coa roa acc tgo acc otg gaa coa gga gtg gac cot acc Ala Pro Xaa Pro Xaa Thr Cys Thr Leu Glu Pro Gly Val Asp Pro Thr	400
75 80 85	
cga set gte tgt att aat eee cat eee eea eea ate tta aaa abe	536
Arg Xaa Val Cys Ile Asn Pro His Pro Pro Pro Pro Ile Leu Lys (aa	
90 95 100	
cot otg too coc tac cot aaa coc cag tta ggt acc cat got ggg caa	584
Pro Leu Ser Pro Tyr Pro Lys Pro Gln Leu Gly Thr His Ala Gly Gln	
105 110 115	
gtc aat taacaattta tgcacaggta ctagttttat tgtattaccg ttccagggta	640
Val Asn	
120	
gctttgaaaa aagtatetea aaaaggcaae atgggeegag egeagtgget caegeetgta	700
atcccagcac tttgggaggc caaggtgggc agatcgcctg aggtctggag ttcaagacca	760
gcctggccaa cagggtgaaa ccccgtctct acaaaaatar gaaaattrgc caggtgtggt	820
ggcagacgtc tgtrgtccca gctattcagg agactgaggc acgagaattc catgaaccca	880
ggatgcggag gttgcagtga gccgagattg tgccactgcg ctccagcctg ggcgacagag	940
tggtattctg tttcaaaaaa aaaaamcm	968
<pre>&lt;210&gt; 337 &lt;211&gt; 901 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 133846  &lt;221&gt; sig_peptide &lt;222&gt; 133345 &lt;223&gt; Von Heijne matrix</pre>	
400 - 227	
<400> 337 aagcagette caggateetg agateeggag cageeggggt eggagegget ceteaagagt	60
tactgatcta thhatggcag agaaaaaaa attgtgacca gagacgtgta gcaatgaaca	120
aggaacrtca ta atg rwn nnk ttc aca gac ccc tct tca gtg aat gaa aag	171
Met Xaa Xaa Phe Thr Asp Pro Ser Ser Val Asn Glu Lys	
-70 -65 -60	
aag agg agg gag cgg gaa gaa agg cag aat att gto ctg tgg aga cag	219
Lys Arg Arg Glu Arg Glu Glu Arg Gln Asn Ile Val Leu Trp Arg Gln	
-55 -50 -45	
- 33	
cog etc att acc ttg cag tat ttt tet etg gaa ate ett gta ate ttg	267

Pro	Leu	Ile -40	Thr	Leu	Gln	Tyr	Phe	Ser	Leu	Glu	Ile	Leu -30	Val	Ile	Leu	
aag	gaa	tgg	acc	tca	aaa	tta	tgg	cat	cgt	caa	agc	att	gtg	gtg	tct	315
Lys	Glu	Trp	Thr	Ser	Lys	Leu	Trp	His	Arg	Gln	Ser	Ile	Val	Val	Ser	
	-25					-20					-15					
			ctg													363
Phe	Leu	Leu	Leu	Leu	Ala	Gly	Leu	Ile	Ala	Thr	Tyr	Tyr	Val	Glu	Gly	
-10					- 5					1				5		
			cag													411
Val	His	Gln	Gln	Tyr	Val	Gln	Arg		Glu	Lys	Gln	Phe		Leu	Tyr	
			10					15					20			
			ata													459
Ala	Tyr	_	Ile	Gly	Leu	Gly		Leu	Ser	Ser	Val		Leu	GIÀ	Thr	
		25					30					35				
			acc													507
Gly		His	Thr	Phe	Leu		Tyr	Leu	Gly	Pro		IIe	Ala	ser	Val	
	40		•			45					50					
			gct													555
	Leu	Ala	Ala	Tyr		Cys	Asn	Ser	Val		Phe	Pro	Glu	Pro		
55					60					65					70	603
tat	cct	gat	cag	att	att	tgt	cca	gat	gaa	gag	ggc	act	gaa	gga	acc	603
Tyr	Pro	Asp	Gln		Ile	Cys	Pro	Asp		Glu	GIÀ	Thr	GIU		Inr	
				75					80		- 4- 4-			85		657
			tgg													651
Ile	Ser	Leu	Trp	Ser	Ile	He	ser		Val	Arg	me	GIU		Cys	Met	
			90		•			95					100			699
tgg	ggt	atc	ggt	aca	gca	atc	gga	gag	ctg	CCE	cca	tat	משם	acg	gee	033
Trp	Gly		Gly	Thr	Ala	, iie		GIU	Leu	Pro	PTO		Pne	met	Ala	
		105					110				·	115				747
aga	gca	gct	cgc	ctc	tca	ggt	gct	gaa	cca	gat	gat	gaa	gag	Tat	cag	/42/
Arg		Ala	Arg	Leu	Ser		Ala	GIU	PTO	Asp			GIU	LYL	Gln	
	120					125					130		~+~	200	2.63	795
gaa	ttt	gaa	gag	atg	ctg	gaa	cat	gca	gag	CCL	gca	caa	gta	aga	aca	193
	Phe	Glu	Glu	Met		GIU	HIS	АТА	GIU			GIN	Vai	Arg	Thr 150	
135					140					145						843
gtg	<b>aa</b> a	ata	gaa	aat	aga	aca	CEE	tac	משם	כנכ	cta	aag	agg	Tou	tta Lev	043
Val	GIY	IIe	GIu			Tnr	Leu	Tyr		rne	ren	: PA8	MIG	165	Leu	
				155					160							901
	taa	aatt	gtt	agta	gtta	CE C	tgaa	gaag	a aa	actg	ctaa	agt	aaaa	add	aaaaa	301
Arg																

<221> polyA_site

<222> 1338..1347

-400	0 > 3	2 9														
			rgaa	agtac	מר א	ctaa	agto	aca	atat	ttc	ttct	дааа	itt c	tcad	gcagt	60
															ggaat	120
														gaa a		170
-	5		ـ د د د	۱ –د،	det (	ilu A	ara G	iln s	er A	irq V	al M	let S	er c	lu L	ys.	
							.35					-30			•	
gat	gag	tat	cag	ttt	caa	cat	cag	gga	gcg	gtg	gag	ctg	ctt	gtc	ttc	218
Asp	Glu	Tyr	Gln	Phe	Gln	His	Gln	Gly	Ala	Val	Glu	Leu	Leu	Val	Phe	
•	-25	•				-20		•			-15					
aat	ttt	ttg	ctc	atc	ctt	acc	att	ttg	aca	atc	tgg	tta	ttt	aaa	aat	266
Asn	Phe	Leu	Leu	Ile	Leu	Thr	Ile	Leu	Thr	Ile	Trp	Leu	Phe	Lys	Asn	
-10					- 5					1				5		
cat	cga	ttc	cgc	ttc	ttg	cat	gaa	act	gga	gga	gca	atg	gtg	tat	ggc	314
His	Arg	Phe	Arg	Phe	Leu	His	Glu		Gly	Gly	Ala	Met		Tyr	Gly	
			.10					15					20			262
ctt	aya	atg	gga	cta	att	tta	csa	tat	gct	aca	gca	cca	act	gat	272 730	362
Leu	Xaa		Gly	Leu	Ile	Leu		Tyr	Ala	Thr	Ala	Pro	Thr	Asp	11e	
		25					30					35				410
gaa	agt	ggr	rct	gtc	tat	gac	tgt	gta	aaa	Cta	act	Dha	agi	cca	Cor	410
GIU		GIÀ	хаа	vai	Tyr		Cys	vai	гуя	Leu	50	PHE	361	Pro	261	
	40					45	<b>~</b> 3.6	C 2 2	a++	tat		tat	222	tac	aar	458
The	Len	Lou	Val	Aar Aar	Tla	Thr	Aen	Gln	Val	Tvr	Glu	Tvr	Lvs	Tyr	Lvs	•••
55	neu	rea	val	ASII	60	1111	vaħ	GIII	Vai	65	014	.,.	<i>D</i>	- / -	70	
	gaa	ata	agt	cad		amc	atc	aat	cct		cam	gga	aat	gct	_	506
Ara	Glu	Tle	Ser	Gln	His	Xaa	Tle	Asn	Pro	His	Xaa	Glv	Asn	Ala	Ile	
			-	75					80		••••	1		85		
ctt	gaa	aag	ato		ttt	gat	cca	raa	atc	ttc	ttc	aat	gtt	tta	ctg	554
Leu	Glu	Lvs	Met	Thr	Phe	Asp	Pro	Xaa	Ile	Phe	Phe	Asn	Val	Leu	Leu	
		4	90			•		95					100			
cca	cca	att	ata	ttt	cat	gca	gga	tat	agt	cta	aag	aag	aga	cac	ttt	602
Pro	Pro	Ile	Ile	Phe	His	Ala	Gly	Tyr	Ser	Leu	Lys	Lys	Arg	His	Phe	
		105					110					115				
ttt	caa	aac	tta	gga	tct	att	tta	acg	tat	gcc	ttc	ttg	gga	act	gcc	650
Phe	Gln	Asn	Leu	Gly	Ser	Ile	Leu	Thr	Tyr	Ala	Phe	Leu	Gly	Thr	Ala	
	120					125					130					
								gtga	cat	tcgg	agct	ca a	gttg	cagg	t	701
	Ser	Cys	Ile	Val		Gly										
135					140											761
ggc	tgtg	<b>99</b> 9	tcyg	tgat	ct g	tgtg	aggg	a tc	taac	actt	cca	ggat	CCC	Eget	ggckgg	821
gaaa	aatt	gtc	tttt	tttt	ar t	awat	caca	w at	ttgt	atgt	כככ	ECCW	gae	ccaa	ttccac	881
ggc	ttck	gam	aaat	acaa	gg c	ttca	aatc	a aa	gcaa	acta	wag	gatt	get	tato	tttctc	941
tgt	gagt	tct	ggac	ttct	ga c	ttag	ggaa	t gt	ggat	cact	tge	ctos	ayu	cett	tgaagc	1001
gca	ttgc	att 	CTTC		ag t	ctga atat	ytaa ++~~	. SC	cyat	acyc	220	taan	tat	atac	tttgtc	1061
crg.	-a	yag	agac	ctta ann	20 C	yıac +	2020	- ag	yayı	yuad tass	aay	caat =	tat	CCAR	caagag atatca	1121
כככ		tee	aaag	yaaa taa	9t t	arac	ayac	- yc	ayıc	atan	cct	gata	aat	acac	actett	1181
aca:	yagc	tta	tudd tatt	rece	99 9 50 3	atay	acra	c to	agen	ctas	atr	acac	att	atat	actctg	1241
~~+	taan	act	catt	2122	eg a	2222	rata	ia te	CCSS	aton	taa	agge	aat	ccac	cctctg	1301
317	stca	cat	ccaa	race	ey ,t	2200	tcca	ic to	cage	aaaa	aaa	aaa			,	1347
ald	مردر ا	-yı	aa			augu				,						

<210> 339

<211> 987

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

```
<222> 124..411
<221> sig_peptide
<222> 124..186
<223> Von Heijne matrix
     score 6.30000019073486
     seq MVALCCCLWKISG/CE
<221> polyA_signal
<222> 948..953
<221> polyA site
<222> 971..983
<400> 339
aagacgctgc ctttagggag agataaaaag cataatgaca ttagctagga aagttaattt
                                                                      60
tcagttctta ctgaagtgct gtatgaaact gaaatttcca aggaactgaa ttttgtgagc
                                                                     120
caa atg agc atg caa ttc ttg ttt aag atg gtg gcc tta tgc tgt tgt
                                                                     168
   Met Ser Met Gln Phe Leu Phe Lys Met Val Ala Leu Cys Cys
                                                -10
                                                                     216
ctc tgg aag atc tcc ggc tgt gag gaa gtc cct cta act tac aac ctg
Leu Trp Lys Ile Ser Gly Cys Glu Glu Val Pro Leu Thr Tyr Asn Leu
   - 5
                       1
                                                                     264
ctc aag tgc ctc cta gat aaa gcg cac tgt gta ctc ctg aca cct tgt
Leu Lys Cys Leu Leu Asp Lys Ala His Cys Val Leu Leu Thr Pro Cys
                                    20
               15
                                                                     312
ggt tac atc ttt tcc ttg atc agt cca gaa att ctc aaa ctc act tta
Gly Tyr Ile Phe Ser Leu Ile Ser Pro Glu Ile Leu Lys Leu Thr Leu
           30
                                35
atc act ttg cav atc ctc tta ata ctc aaa aat cta cac tta ctg tgg
                                                                     360
Ile Thr Leu Xaa Ile Leu Leu Ile Leu Lys Asn Leu His Leu Leu Trp
                           50
                                                55
                                                                     408
ctg aca gtt tca agc awa tgt gtt cat cgc agt agt gca aga aaa gaa
Leu Thr Val Ser Ser Xaa Cys Val His Arg Ser Ser Ala Arg Lys Glu
                        65
aag tagaagaacc ctgcagagat ttgatggaac ccagcttcta ttcattaaaa
                                                                     461
Lys
ccaatggcaa aatataaagc aaataggagg tgacgaaggt tacaaaaata cgtattgttt
atgttttccc tggggtgtgc tgattgtcag gcatcagttc cctgtgccat tcattcccca
acacagcatg catcagaaat tttatcaata aatgctttct ctctcaatgt tcaacctatg
                                                                     641
ctgatagacc attaaataca gtttttgggt tcacagcttg tcatcatcat ttgtctatac
                                                                     701
ctgtggcaaa gaatatctaa taagatactc tcagcatttt gcacacttaa actaagatgc
                                                                     761
                                                                     821
tgaatgctgt attttacgga ataatcagcc acattaaatt tggagactca acaagcatgc
                                                                     881
tgtgaacatt caacattagg tttaaatttt atttttaaaa gttaataata aaaggatata
tgttaagtat tatgaaaccc tgcatatact gtaataaaat ggtggatgtg aatggacaat
                                                                      941
                                                                      987
atatgcaata aaatttataa tttgattcya aaaaaaaaa aamccv
```

```
<211> 748
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 372..494
```

<210> 340

<221> sig_peptide <222> 372 .443

<223> Von Heijne matrix

## score 5.30000019073486 seq RILLLHFYCLLRS/SE

<221> polyA_signal <222> 708..713 <221> polyA site <222> 732..745 <400> 340 acatgaaatg tgcttggtct gtgatctctt ggtcagatat ctgccttcca ggcgatcctt tgaggttgtg taattcagct ggccctggct cctggtccct gttactgagc tgggcagtcg 120 aaccgaaggc agatgagctc aagatcatgc cttgggaagc atggtgctct aggggtgcct 180 ttttattcct ttcattgtat tatagactgt ttccaagttt atggttagaa atggtaaagt 240 gggtctggtg ttttgaggta gaacccagcc tagggcaaga tatgaactgt tcttgaggta qaaatgtcta cagtcagttg tttcatctag cttgcatctt aaaacacaaa cccttcagtt gettteaett a atg cae aca tit gee aat gae aga ggg tia tae agg ate Met His Thr Phe Ala Asn Asp Arg Gly Leu Tyr Arg Ile -20 ctt ctt tta cat ttc tat tgt ctg cta cgc tca tca gag tat att ttg Leu Leu Leu His Phe Tyr Cys Leu Leu Arg Ser Ser Glu Tyr Ile Leu -10 - 5 1 ggg tac aag gtt ttg ggg gtt ttt tty ccc att ttg taactgcctt 504 Gly Tyr Lys Val Leu Gly Val Phe Phe Pro Ile Leu 10 15 attgaaaadt aaktgeeett eeatteeagg eeteeteata ttgtaettgt tteetgeeaa 564 atctggggga tcatttgtat tttaactttg taatctatgg ctctgtactg ttgaaagstc 624 tcaattctgt ggggtctcct tagtatgtat gtgacttttc atgttgcaat atcacacgat 684 gggatggccc gacttttgct cttaataaat aatctgaatg agtaagaraa aaaaaaaaaa 744 748 accc

<210> 341

<211> 1106

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 112..450

<221> sig_peptide

<222> 112..192

<223> Von Heijne matrix
score 7.19999980926514
seq SLLFFLLLEGGXT/EQ

<221> polyA_signal

<222> 1053..1058

<221> polyA site

<222> 1095..1106

<400> 341

															acgga Jaga	60 117
raa	aag	tgg	aaa	atg	gga	ggc	atg	aa <b>a</b>	tac	atc	ttt	tcg	ttg	ttg	ttc	165
-25					-20	Gly				-15					-10	213

```
Phe Leu Leu Glu Gly Gly Xaa Thr Glu Gln Val Xaa His Ser Glu
aca tat tgc atg ttt caa gac aag aag tac aga gtg ggt gag aga tgg
                                                                     261
Thr Tyr Cys Met Phe Gln Asp Lys Lys Tyr Arg Val Gly Glu Arg Trp
                           15
cat cct tac ctg gaa cct tat ggg ttg gtt tac tgc gtg aac tgc atc
                                                                     309
His Pro Tyr Leu Glu Pro Tyr Gly Leu Val Tyr Cys Val Asn Cys Ile
                       30
tgc tca gag aat ggg aat gtg ctt tgc agc cga gtc aga tgt cca aat
                                                                     357
Cys Ser Glu Asn Gly Asn Val Leu Cys Ser Arg Val Arg Cys Pro Asn
                   45
                                        50
gtt cat tgc ctt tct cct gtq cat att cct cat ctq tqc tgc cct cgc
                                                                     405
Val His Cys Leu Ser Pro Val His Ile Pro His Leu Cys Cys Pro Arg
                60
                                    65
                                                                     450
tgc cca gaa gac tcc tta ccc cca gtg aac aat rwg gtg acc agc
Cys Pro Glu Asp Ser Leu Pro Pro Val Asn Asn Xaa Val Thr Ser
                               80
tagtettgek agtacaatgg gacaacttae caacatggas agetgttegt aget rrggg
                                                                     510
                                                                     570
ctettteaga ateggeaace emateaatge acceagtgea getgttegga rggaaacktg
                                                                     630
tattgtggtc tcaagacttg ccccaaatta acctgtgcct tcccagtctc tgttccarat
tcctgctgcc gggtwtgcag argagatgga caactgtcat gggaacmttc tgatggtgat
                                                                     690
atcttccggc aacctgccaa cagagaagca agacattctt accaccgctc tcactatgat
                                                                     750
cctccaccaa qccqacaqqc tggaggtctg tcccgctttc ctggggccag aagtcaccgg
                                                                     810
                                                                     870
ggagetetta tggatteeca geaageatea ggaaceattg tgeaaattgt cateaataae
aaacacaagc atggacaagt gtgtgtttcc aatggaaaga cctattctca tggcgagtcc
                                                                     930
tggcacccaa acctccgggc atttggcatt gtggagtgtg tgctatgtac ttgtaatgtc
                                                                     990
accaagcaag agtgtaagaa aatccactgc cccaatcgat acccctgcaa gtatcctcaa
                                                                    1050
                                                                    1106
aaaatagacg gaaaatgctg caaggtgtgt ccaggtaaaa aagcaaaaaa aaaaaa
```

```
<210> 342
  <211> 1191
  <212> DNA
. <213> Homo sapiens
  <220>
  <221> CDS
  <222> 117..866
  <221> sig_peptide
  <222> 117..170
  <223> Von Heijne matrix
        score 10.6999998092651
        seq LILLALATGLVGG/ET
   <221> polyA_signal
   <222> 1159..1164
   <221> polyA site
   <222> 1178..1190
```

	ctacctgctg tagcto			
agg att ctg Arg Ile Leu -15	cag tta atc ctg Gln Leu Ile Leu	ctt gct ctg gca Leu Ala Leu Ala -10	aca ggg ctt gta Thr Gly Leu Val -5	ggg 167 Gly
gga gag acc Gly Glu Thr 1	agg atc atc aag Arg Ile Ile Lys 5	ggg ttc gag tgc Gly Phe Glu Cys 10	aag cct cac tcc Lys Pro His Ser	cag 215 Gln 15

	ccc	tgg	cag	gca	gcc	ctg	ttc	gag	aag	acg	cgg	cta	ctc	tgt	999	gcg	263
	Pro	Trp	Gln	Ala	Ala	Leu	Phe	Glu	Lys	Thr	Arg	Leu	Leu	Cys	Gly	Ala	
					20					25 -					30		
									ctg								311
	Thr	Leu	Ile	Ala	Pro	Arg	Trp	Leu	Leu	Thr	Ala	Ala	His	Cys	Leu	Lys	
				35					40					45			
									cag								359
	Pro	Arg	Tyr	Ile	Xaa	His	Leu		Gln	His	Asn	Leu		Lys	Glu	Glu	
٠			50					55					60				
									act								407
	Gly	-	Glu	Gln	Thr	Arg		Ala	Thr	Glu	Ser		Pro	His	Pro	Gly	
		65					70					75					
				_					gac		-		-	_	_	_	455
	Phe	Asn	Asn	Ser	Leu	Pro	Asn	Lys	Asp	Xaa		Asn	Asp	Ile	Met		
	80					85					90					95	
									atc								503
	Val	Xaa	Met	·Xaa		Pro	Val	Ser	Ile		Trp	Ala	Val	Arg		Leu	
					100					105					110		
									gct								551
	Thr	Leu	Ser	Ser	Arg	Cys	Val	Thr	Ala	Gly	Thr	Ser	Cys		Ile	Ser	
				115					120					125			
	ggc	tgg	ggc	agc	acg	tcc	agc	CCC	cag	tta	cgc	ctg	cct	cac	acc	ttg	599
	Gly	Trp	Gly	Ser	Thr	Ser	Ser		Gln	Leu	Arg	Leu		His	Thr	Leu	
			130					135					140				
									gag								647
	Arg	Сув	Ala	Asn	Ile	Thr		Ile	Glu	His	Gln		Cys	Glu	Asn	Ala	
		145					150					155					
									atg								695
	-	Pro	Gly	Asn	Ile		Asp	Thr	Met	Val		Ala	Ser	Val	GIn		
	160					165					170					175	
	ggg	ggc	aag	gac	tcc	tgc	cag	ggt	gac	tcc	999	ggc	cct	ctg	gtc	tgt	743
	Gly	Gly	Lys	Asp		Cys	Gln	Gly	Asp		Gly	Gly	Pro	Leu	Val	Сув	
					180					185					190		
	aac	cag	tct	ctt	caa	ggc	att	atc	tcc	tgg	ggc	cag	gat	ccg	tgt	gcg	791
	Asn	Gln	Ser	Leu	Gln	Gly	Ile	Ile		Trp	Gly	Gln	Asp		Сув	Ala	
				195					200					205			
	atc	acc	cga	aag	cct	ggt	gtc	tac	acg	aaa	gtc	tgc	aaa	tat	gtg	gac	839
	Ile	Thr	Arg	Lys	Pro	Gly	Val		Thr	Lys	Val	Cys			Val	Asp	
			210					215					220				
									aat	tag	actg	gac	ccac	ccac	ca		886
	Trp	Ile	Gln	Glu	Thr	Met	Lys	Asn	Asn								
		225					230										
	cago	ccat	tca d	ccct	ccat	tt c	cact	tggt	g tt	tggt	tcct	gtt	cact	ctg	ttaa	taagaa	946
	acco	taaq	gcc a	aaga	ccct	ct a	cgaa	catt	c tt	tggg	cctc	ctg	gact	aca	ggag	atgctg	1006
	tcad	cttaa	ata a	atca	acct	gg g	gttc	gaaa	t ca	gtga	gacc	tgg	attc	aaa	ttct	gccttg	1066
	aaat	atte	gtg a	actc	tggg	aa t	gaca	acac	c tg	gttt	gttc	tct	gttg	tat	cccc	agcccc	1126
	aaa	cwca	gct (	cctg	gcca	ta t	atca	aggt	t tc	aata	aata	ttt	gcta	aat	gaaw	aaaaaa	1186
	aaaa	ac .															1191

<210> 343

<211> 1070

<212> DNA

<213> Homo sapiens

<220>

<221> CDS <222> 13..465

<221> sig_peptide <222> 13..75

<223> Von Heijne matrix score 3.90000009536743 seq PVAVTAAVAPVLS/IN

<221> polyA_signal <222> 1035..1040

<221> polyA_site <222> 1060..1070

<400> 343	٠				
agagtcggga aa a		-		tg gct gtg acg al Ala Val Thr	51
	-20	-	15	-10	
gcg gca gtg gcg	cct gtc ctg	tcc ata aac	agc gat tto	tca gat ttg	99
Ala Ala Val Ala				_	
√ <b>-</b> 5		1	- 5		
cgg gaa att aaa	aag caa ct	ctg ctt att	gcg ggc ctt	acc cgg gag	147
Arg Glu Ile Lys	Lys Gln Let	Leu Leu Ile	Ala Gly Leu	Thr Arg Glu	
10	15		20		
cgg ggc cta cta	cac agt ago	aaa tgg tcg	gcg gag ttg	get tte tet	195
Arg Gly Leu Leu	His Ser Ser	Lys Trp Ser	Ala Glu Leu	Ala Phe Ser	
25	30	-	35	40	
ctc cct gca ttg	cct ctg gc	gag ctg caa	ccg cct ccg	cct att aca	243
Leu Pro Ala Leu					
	45	50		55	
gag gaa gat gco	cag gat at	g gat gcc tat	acc ctg gcc	aag god tac	291
Glu Glu Asp Ala					
60		65		70	
ttt gac gtt aaa	qaq tat gai	cgg gca gca	cat ttc ctc	cat ggc tgc	339
Phe Asp Val Lys	Glu Tyr Ası	Arg Ala Ala	His Phe Lev	His Gly Cys	
75	•	80	85		
aat gca aga aaa	qcc tat tti	t ctg tat atg	tat tcc aga	tat ctg gtg	387
Asn Ala Arg Lys					
90	95	•	100		
agg gcc att tta	aaa tgt ca	t tet gee ttt	agt gaa aca	tcc ata ttt	435
Arg Ala Ile Leu	Lys Cys Hi	s Ser Ala Phe	Ser Glu Thi	Ser Ile Phe	
105	110		115	120	
aga acc aat gga	aaa gtt aa	a tct ttt aaa	tagcttagca	gtgggccact	485
Arg Thr Asn Gly					
	125	130			
gaatgaatgt actt	tataca tago	aataat aaaaaa	aaga tatcata	aaat aaagttaaaa	545
aggatggtaa aaaa					605
atttatttac ttta					665
gaattaagtt aaaa					725
				taaa ggacaatgca	785
agtaaaccaa ctta					845
				attg attaaaaaaa	905
				tttg aagtgcttgg	965
gaccaaaagt gttt					1025
				cera carranaere	1070
actggttgaa ataa	idadaty ctgc	ayiyay iyica	iaada dadda		1070

<210> 344

<211> 1213

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 2..718

<221> sig peptide <222> 2..76 <223> Von Heijne matrix score 3.90000009536743 seg RVGLLLGGGGVYG/SR <221> polyA signal <222> 1170..1175 <221> polyA_site <222> 1203..1213 <400> 344 a atg ccc cgg aag cgg aag tgc gat ctt cgg gct gtc aga gtt ggt ctg 49 Met Pro Arg Lys Arg Lys Cys Asp Leu Arg Ala Val Arg Val Gly Leu -20 tta ctc gqt gqt ggc gga gtc tac gga agc cgt ttt cgc ttc act ttt 97 Leu Leu Gly Gly Gly Val Tyr Gly Ser Arg Phe Arg Phe Thr Pae - 5 cct ggc tgt aga gcg ctt tcc ccc tgg cgg gtg aga vtg cag aga cga Pro Gly Cys Arg Ala Leu Ser Pro Trp Arg Val Arg Xaa Gln Arg Arg 15 20 agg tgc gag atg agc act atg ttc gcg gac act ctc ctc atc gtt ttt 193 Arg Cys Glu Met Ser Thr Met Phe Ala Asp Thr Leu Leu Ile Val Phe 25 30 35 241 ate tet gtg tge acg get etg etc gea gag gge ata ace tgg gte etg Ile Ser Val Cys Thr' Ala Leu Leu Ala Glu Gly Ile Thr Trp Val Leu 45 50 289 gtt tac agg aca gac aag tac aag aga ctg aag gca gaa gtg gaa aaa Val Tyr Arg Thr Asp Lys Tyr Lys Arg Leu Lys Ala Glu Val Glu Lys 65 60 cag agt aaa aaa ttg gaa aag aag gaa aca ata aca gag tca gct 337 Gln Ser Lys Lys Leu Glu Lys Lys Lys Glu Thr Ile Thr Glu Ser Ala 75 80 85 ggt cga caa cag aaa aar aaa ata gag aga cdd kaa kas amc ctg arg Gly Arg Gln Gln Lys Lys Lys Ile Glu Arg Xaa Xaa Xaa Leu Xaa 95 aat aac aac aga gat cta tca atg gtt cga atg aaa tcc atg ttt gct 433 Asn Asn Asn Arg Asp Leu Ser Met Val Arg Met Lys Ser Met Phe Ala 110 115 att ggc ttt tgt ttt act gcc cta atg gga atg ttc aat tcc ata ttt Ile Gly Phe Cys Phe Thr Ala Leu Met Gly Met Phe Asn Ser Ile Phe 125 130 gat ggt aga gtg gtg gca aag ctt cct ttt acc cct ctt tct tas rtc 529 Asp Gly Arg Val Val Ala Lys Leu Pro Phe Thr Pro Leu Ser Xaa Xaa 140 577 sra gga ctg tct cat cga aat ctg ctg gga gat gac acc aca gac tgt Xaa Gly Leu Ser His Arg Asn Leu Leu Gly Asp Asp Thr Thr Asp Cys 160 tcc ttc att ttc ctg taw att ctc tgt act atg tcg att cga cag aac 625 Ser Phe Ile Phe Leu Xaa Ile Leu Cys Thr Met Ser Ile Arg Gln Asn 170 175 att cag aag att ete gge ett gee eet tea ega gee gee aee aag eag 673 Ile Gln Lys Ile Leu Gly Leu Ala Pro Ser Arg Ala Ala Thr Lys Gln 190 195 718 gca ggt gga ttt ctt ggc cca cca cct cct tct ggg aag ttc tct Ala Gly Gly Phe Leu Gly Pro Pro Pro Pro Ser Gly Lys Phe Ser 210 205 tgaactcaag aactctttat tttctakcat tctttctaga cacacacaca tcagactggc 778 aactgttttg tascaagage cataggtage ettackaett gggeetettt etagttttga 838 attatttcta agccttttgg gtatkattag agtgaaaatg gcagccagca aacttgatag 898

```
tgcttttggt cctagatgat ttttatcaaa taagtggatt gattagttaa gttcaggtaa
tgtttatgta atgaaaaaca aatagcatco ttottgttto atttacataa gtattttotg
                                                                    1018
tgggaccgac tctcaaggca ctgtgtatgc cctgcaagtt ggctgtctat gagcatttag
                                                                    1078
agatttagaa gaaaaattta gtttgtttaa cccttgtaac tgtttgtttt gttgttgttt
                                                                    1138
ttttttcaag ccaaatacat gacataarat caataaarag gccaaatttt tasctgtttt
                                                                   1198
                                                                    1213
atgtaaaaaa aaaaa
<210> 345
<211> 978
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 86..709
<221> sig_peptide
<222> 86..361
<223> Von Heijne matrix
     score 6.30000019073486
      seq LLMSILALIFIMG/NS
<221> polyA_signal
<222> 943..948
<221> polyA_site
<222> 963..973
<400> 345
aaagcatcct tccctaggac tgctgtaagc ttttgagcctc tagcaggaga catgcctcgg
ggacgaaaga gtcggcgccg ccgta atg cga gag ccg cag aag aga acc gca
                                                                      112
                            Met Arg Glu Pro Gln Lys Arg Thr Ala
                                     -90
                                                                      160
aca atc gca aaa tyc rrg gcs tva gag ggc ctc cga gac ccc tat ggc
Thr Ile Ala Lys Xaa Xaa Ala Xaa Glu Gly Leu Arg Asp Pro Tyr Gly
                                -75
            -80
cgc ctc tgt ggt agc gag cac ccc cga aga cca cct gag cgg ccc gag
                                                                      208
Arg Leu Cys Gly Ser Glu His Pro Arg Arg Pro Pro Glu Arg Pro Glu
        -65
                                                                      256
qua que ceg age act cea gag gag gee tet ace ace cet gaa gaa gee
Glu Asp Pro Ser Thr Pro Glu Glu Ala Ser Thr Thr Pro Glu Glu Ala
                        -45
tog ago act goo caa goa caa aag cot toa gtg coo cgg ago aat ttt
                                                                      304
Ser Ser Thr Ala Gln Ala Gln Lys Pro Ser Val Pro Arg Ser Asn Phe
                    -30
                                        -25
cag ggc acc aag aaa agt ctc ctg atg tct ata tta gcg ctc atc ttc
                                                                      352
Gln Gly Thr Lys Lys Ser Leu Leu Met Ser Ile Leu Ala Leu Ile Phe
                                     -10
                -15
atc atg ggc aac agc gcc aag gaa gct ctg gtc tgg aaa gtg ctg ggg
Ile Met Gly Asn Ser Ala Lys Glu Ala Leu Val Trp Lys Val Leu Gly
                                                10
                                                                      448
aag tta gga atg cag cct gga cgt cas cac agc atc ttt gga gat ccg
Lys Leu Gly Met Gln Pro Gly Arg Xaa His Ser Ile Phe Gly Asp Pro
                        20
aag aar atc gtc aca gaa ran ttt gtg cgc aga ggg tac ctg att tat
                                                                       496
Lys Lys Ile Val Thr Glu Xaa Phe Val Arg Arg Gly Tyr Leu Ile Tyr
                                        40
                    35
ara ccg gtg ccc cgt abc agt ccg gtg gag tat gas ttc ttc tgg ggg
                                                                      544
Xaa Pro Val Pro Arg Xaa Ser Pro Val Glu Tyr Xaa Phe Phe Trp Gly
```

WO 99/31236 -262- PCT/IB98/02122

Pro Arg Ala His Val Glu Ser Ser Xaa Leu Lys Xaa Xaa His Phe Val 65 70 75	592
gca agg gtt cgt aac cga tgc tct aaa gac tgg cct tgt aat tat gac Ala Arg Val Arg Asn Arg Cys Ser Lys Asp Trp Pro Cys Asn Tyr Asp 80 85 90	640
tgg gat tcg gac gat gat gca gag gtt gag gct atc ctc aat tca ggt Trp Asp Ser Asp Asp Asp Ala Glu Val Glu Ala Ile Leu Asn Ser Gly 95 100 105	688
get arg ggt tat tee gee eet taagtarate tgaggeagae eettgggggt Ala Xaa Gly Tyr Ser Ala Pro 110 115	739
gtaaaagaga gtcacaggta ccccaaggag tagatgccag ggtcctaagt tgaaaatgmt gtcgattggg ggcgggggac actgtatttg atatttgtga tcagtgatca ttgttcaact gcgaaataga gtgtttgctt ttgataatgg aaaattgtat tcgttttaaa attccgtttg ttgagaataa caatatgttt aaaaatataa ttgaacaaat tttaaaaaaa aaaamcccy	799 859 919 978
	370
<210> 346 <211> 810 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 63320	
<221> sig_peptide <222> 63179 <223> Von Heijne matrix score 3.90000009536743 seq VLAIGLLHIVLLS/IP	
<221> polyA_signal	
<221> polyA_site <222> 799810	
<400> 346 agggaaccga tcccgggccg ttgatcttcg gccccacacg aacagcagag aggggcatca gg atg aat gtk ggc aca gcg cac ags dag gtg aac ccc aac acg cgg Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg -35 -25	60 107
agggaaccga tecegggeeg ttgatetteg geeccacaeg aacageagag aggggeatea gg atg aat gtk gge aca geg cae ags dag gtg aac eee aac aeg egg	
agggaaccga tcccgggccg ttgatcttcg gccccacacg aacagcagag aggggcatca gg atg aat gtk ggc aca gcg cac ags dag gtg aac ccc aac acg cgg Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg -35 -30 -25 gtk atg aac agc cgt ggc atc tgg ctc tcc tac gtg ctg gcc atc ggt Val Met Asn Ser Arg Gly Ile Trp Leu Ser Tyr Val Leu Ala Ile Gly	107
agggaaccga tcccgggccg ttgatcttcg gccccacacg aacagcagag aggggcatca gg atg aat gtk ggc aca gcg cac ags dag gtg aac ccc aac acg cgg  Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg  -35  -30  -25 gtk atg aac agc cgt ggc atc tgg ctc tcc tac gtg ctg gcc atc ggt Val Met Asn Ser Arg Gly Ile Trp Leu Ser Tyr Val Leu Ala Ile Gly  -20  -15  ctc ctc cac atc gtg ctg agc atc ccg ttt gtk agt gtc cct gtc Leu Leu His Ile Val Leu Leu Ser Ile Pro Phe Val Ser Val Pro Val	107
agggaaccga tcccgggccg ttgatcttcg gccccacacg aacagcagag aggggcatca gg atg aat gtk ggc aca gcg cac ags dag gtg aac ccc aac acg cgg  Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg  -35  -30  -25  gtk atg aac agc cgt ggc atc tgg ctc tcc tac gtg ctg gcc atc ggt Val Met Asn Ser Arg Gly Ile Trp Leu Ser Tyr Val Leu Ala Ile Gly  -20  -15  ctc ctc cac atc gtg ctg ctg agc atc ccg ttt gtk agt gtc cct gtc Leu Leu His Ile Val Leu Leu Ser Ile Pro Phe Val Ser Val Pro Val  -5  gtc tgg acc ctc acc aac ctc att cac aac atg ggc atg tat atc ttc Val Trp Thr Leu Thr Asn Leu Ile His Asn Met Gly Met Tyr Ile Phe	107 155 203
agggaaccga tcccgggccg ttgatcttcg gccccacacg aacagcagag aggggcatca gg atg aat gtk ggc aca gcg cac ags dag gtg aac ccc aac acg cgg Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg  -35  -30  -25  gtk atg aac agc cgt ggc atc tgg ctc tcc tac gtg ctg gcc atc ggt Val Met Asn Ser Arg Gly Ile Trp Leu Ser Tyr Val Leu Ala Ile Gly  -20  -15  ctc ctc cac atc gtg ctg ctg agc atc ccg ttt gtk agt gtc cct gtc Leu Leu His Ile Val Leu Leu Ser Ile Pro Phe Val Ser Val Pro Val  -5  gtc tgg acc ctc acc aac ctc att cac aac atg ggc atg tat atc ttc Val Trp Thr Leu Thr Asn Leu Ile His Asn Met Gly Met Tyr Ile Phe  10  ctg cac acg gtg aag ggg aca ccc ttt gag acc ccg gac cag ggc aag Leu His Thr Val Lys Gly Thr Pro Phe Glu Thr Pro Asp Gln Gly Lys	107 155 203 251

ccccaagetg ccccagetce aeggakteeg gatttttgga atcaataakt aetgaaaktg

```
casccccttc ccctgcccag ggtggcaggg gaggggtagg gtaaaaggca tktgctgcaa
                                                                     590
                                                                      650
chetgaaaac araaaraara rseetetgga caetgecara ratgggggtt gageetetgg
                                                                     710
cetaatttee eccetegett ecceeagtag ecaacttgga gtagettgta ytggggttgg
ggtaggcccc ctgggctctg accttttctg aattttttga tcttttcctt ttgctttttg
                                                                     770
aatararact ccatggagtt ggtcatggaa aaaaaaaaa
                                                                      810
<210> 347
<211> 771
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 299..418
<221> sig_peptide
<222> 299..379
<223> Von Heijne matrix
      score 3.59999990463257
      seq LTLLLITPSPSPL/LF
<221> polyA_signal
<222> 739..744
<221> polyA_site
<222> 762..771
<400> 347
                                                                      60
accttgggct ccaaattcta gctcataaag atgcaagtkt tgcaatttcc tataaatggt
                                                                      120
taagaaaaga gcaagctgtc cagagagtga gaagtttgaa aagagaggtg cataagagag
                                                                      180
aaatgatgtc catttgagcc ccaccacgga ggttatgtgg tcccaaaagg aatgatggcc
                                                                      240
aagcaattaa tttttcctcc tagttcttag cttgcttctg cattgattgg ctttacacaa
ctggcattta gtctgcatta cacaaataga cactaattta tttggaacaa gcagcaaa
                                                                      298
atg aga act tta ttt ggt gca gtc agg gct cca ttt agt tcc ctc act
                                                                      346
Met Arg Thr Leu Phe Gly Ala Val Arg Ala Pro Phe Ser Ser Leu Thr
         -25
                             -20
 ctg ctt cta atc acc cct tct ccc agc cct ctt cta ttt gat aga ggt
 Leu Leu Leu Ile Thr Pro Ser Pro Ser Pro Leu Leu Phe Asp Arg Gly
                                             1
                         -5
 ctg tcc ctc aga tca gca atg tct tagcccctct cctctctcc attccttcct
                                                                       448
Leu Ser Leu Arg Ser Ala Met Ser
                 10
                                                                       508
gttggtactc atttcttcta acttttaata aacatttagg tataatacat tacagtaagt
                                                                       568
gctatttaga tacaaactta aaacatacta tatattttaa ggatctaaga atcctttara
                                                                       628
 rrrggcacat gactgaagta cctcagctgc gcagcctgta accagttttt ttaatgtaaa
 agtaaraatg ccagccttaa cctabccctg carataaaag ctaactttta ttaataccag
                                                                       688
 ccctgaataa tggcactaat ccacactctt ccttaragtg atgctggaaa aataaaatca
                                                                       748
                                                                       771
 ggggcttcag attaaaaaaa aaa
```

<210> 348

<211> 409

<212> DNA

<213 > Homo sapiens

<220>

<221> CDS

<222> 186..380

<221> sig_peptide

```
<222> 186..233
<223> Von Heijne matrix
      score 4
      seq FFLFLSFVLMYDG/LR
<221> polyA_signal
<222> 383..388
<221> polyA_site
<222> 396..409
<400> 348
ataaaagaag cagcaaatag aatttcccac aaagtaagtt gactctaaat cttaagtatt
acctagtttt ttaaaggttt gaatataata atgcagtatt tqcaqtataa aaaggaaqqa
                                                                     120
attigtagag aatcattitg gigcicaagi cicitagcag igccitatig ccicatagca
agaag atg ctg ggg ttt ttt ttg ttt ttg tcc ttt gta tta atg tat gat
                                                                     230
      Met Leu Gly Phe Phe Leu Phe Leu Ser Phe Val Leu Met Tyr Asp
                              -10
                                               - 5
ggt ttg cgc ctt ttt ggc att ctt tca aca tgt cgt qta cat cac acc
                                                                     278
Gly Leu Arg Leu Phe Gly Ile Leu Ser Thr Cys Arg Val His His Thr
                                        10
atg aat cag tto cta att gat ata tot ago ttt acc tcc cga gtt aaa
                                                                     326
Met Asn Gln Phe Leu Ile Asp Ile Ser Ser Phe Thr Ser Arg Val Lys
aaa aaa atc ttt tta ttt tat gcc ttc awa ggt tgc ycg ttt car agt
Lys Lys Ile Phe Leu Phe Tyr Ala Phe Xaa Gly Cys Xaa Phe Gln Ser
                                40
           35
gcc aca taaataaaat gtttaacaaa aaaaaaaaa
                                                                     409
Ala Thr
<210> 349
<211> 613
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 69..458
<221> sig_peptide
<222> 69..233
<223> Von Heijne matrix
      score 4
      seq AALCGISLSQLFP/EP
<221> polyA_signal
<222> 564..569
<221> polyA site
<222> 602..613
<400> 349
aagaacctga gcagcctgtc ttcagacaga gagaggccca cggctgtttc ttgaaaytgg
                                                                       60
                                                                      110
egetggga atg gee atg tgg aac agg eea tgb bag ang etg eet eag eag
         Met Ala Met Trp Asn Arg Pro Xaa Xaa Xaa Leu Pro Gln Gln
                             -50
                                                                      158
cct cts sta gct gag ccc act gca gag ggg gag cca cac ctg ccc acg
Pro Leu Xaa Ala Glu Pro Thr Ala Glu Gly Glu Pro His Leu Pro Thr
```

-40 -35 -30	
-40 -35 -30 ggc cgg gas byg act gag gcc aac cgc ttc gcc tat gct gcc ctc tgt	206
Gly Arg Xaa Xaa Thr Glu Ala Asn Arg Phe Ala Tyr Ala Ala Leu Cys	
-25 -20 -15 -10	
ggc atc tcc ctg tcc cag tta ttt CCt gaa ccc gaa cac agc tcc ttc Gly Ile Ser Leu Ser Gln Leu Phe Pro Glu Pro Glu His Ser Ser Phe	254
-5 1 5	
tgc aca gag ttc atg gca ggc ctg gtg ckm tgg ctg gag ttg tct gaa	302
Cys Thr Glu Phe Met Ala Gly Leu Val Xaa Trp Leu Glu Leu Ser Glu	
10 15 20 gct gtc ttg cca acc atg act gct ttt gcg agc ggc ctg gga ggt gaa	350
Ala Val Leu Pro Thr Met Thr Ala Phe Ala Ser Gly Leu Gly Gly Glu	330
25 30 35	
gga sca vma tgt gtt tgt tca aat ttt act gaa gga ccc cat ctt gaa	398
Gly Xaa Xaa Cys Val Cys Ser Asn Phe Thr Glu Gly Pro His Leu Glu 40 45 50 55	
40 45 50 55 qqa ccc gac ggt gat cac tca gga cct tct gag ctt ctc act caa	446
Gly Arg Pro Asp Gly Asp His Ser Gly Pro Ser Glu Leu Leu Thr Gln	440
60 65 70	
gga tgg gca cta tgacscccgg gccagagtcc tcgtttgcca catgacctcc	498
Gly Trp Ala Leu	
75 ctgctccaag tgcccttgga ggagotggat gtccttgaaa agatgttcct ggagagcotg	558
aaggaaatca aagaagagga atctgaaatg gccgaggcat cccraaaaaa aaaaa	613
<210> 350	
<211> 986	
<212> DNA	
<213> Homo sapiens	
.220	
<220>	•
<220> <221> CDS <222> 12638	
<221> CDS	•
<221> CDS <222> 12638 <221> sig_peptide	
<221> CDS <222> 12638 <221> sig_peptide <222> 12263	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	50
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	50
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	50 98
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	98
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	98
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	98
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	98 146
<pre>&lt;221&gt; CDS &lt;222&gt; 12638  &lt;221&gt; sig_peptide &lt;222&gt; 12263 &lt;223&gt; Von Heijne matrix</pre>	98 146

Tyr	Phe	Leu	Ala -20	Tyr	Leu	Cys	Asn	Ala -15	Gln	Ile	Thr	Met	Leu -10	Gln	Met	
ttq	gca	ctg	ctg	qqc	tat	qqc	ctc	ttt	ggg	cat	tac	att	gtc	ctq	ttc	290
_	•	_	_				Leu				•		_	_		
		- 5		•	•	•	1		-		5					
atc	acc	tat	aat	atc	cac	ctc	cgc	gcc	ctc	ttc	tac	ctc	ttc	tgg	ctq	338
Ile	Thr	Tyr	Asn	Ile	His	Leu	Arg	Ala	Leu	Phe	Tyr	Leu	Phe	Trp	Leu	
10		-			15		_			20	•			-	25	
ttg	gtg	ggt	gga	ctg	tcc	aca	ctg	cgc	atg	gta	gca	gtg	ttg	gtg	tct	386
Leu	Val	Gly	Gly	Leu	Ser	Thr	Leu	Arg	Met	Val	Ala	Val	Leu	Val	Ser	
		•	-	30				_	35					40		
cgg	acc	gtg	ggc	ccc	aca	cad	cgg	mtg	ctc	ctc	tgt	ggc	acc	ctg	gct	434
Arg	Thr	Val	Gly	Pro	Thr	Xaa	Arg	Xaa	Leu	Leu	Cys	Gly	Thr	Leu	Ala	
_			45				-	50			•	•	55			
gcc	cta	cac	atg	ctc	ttc	ctg	ctc	tat	ctg	cat	ttt	gcc	tac	cac	aaa	482
Ala	Leú	His	Met	Leu	Phe	Leu	Leu	Tyr	Leu	His	Phe	Ala	Tyr	His	Lys .	
		60					65	•				70	•		-	
dtg	gta	dag	ggg	atc	ctg	gac	aca	ctg	gag	ggc	ccc	aac	atc	ccg	CCC	530
Xaa	Val	Xaa	Gly	Ile	Leu	Asp	Thr	Leu	Glu	Gly	Pro	Asn	Ile	Pro	Pro	
	75		-			80				_	85					
atc	cag	agg	gtc	CCC	aga	gac	atc	cct	gcc	atg	ctc	cct	gct	gct	cgg	578
Ile	Gln	Arg	Val	Pro	Arg	Asp	Ile	Pro	Ala	Met	Leu	Pro	Ala	Ala	Arg	
90		_			95					100					105	
ctt	ccc	acc	acc	gtc	ctc	aac	gcc	aca	gcc	aaa	gct	gtt	gcg	gtg	acc	626
Leu	Pro	Thr	Thr	Val	Leu	Asn	Ala	Thr	Ala	Lys	Ala	Val	Ala	Val	Thr	
				110					115					120		
ctg	cag	tca	cac	tgad	ccca	acc t	gaaa	attc	tt g	gcca	gtcci	t ct	ttcc	cgca		678
Leu	Gln	Ser	His													
			125													
gctg	gcaga	iga g	gar	jaasa	ac ta	attaa	aagga	a ca	gtcc	tgat	gac	atgt	ttc	gtag	atgggg	738
tttg	cago	tg d	cact	gage	et gi	tage	tgcgt	t aag	gtac	ctcc	ttg	atgc	ctg	tcgg	cacttc	798
															tgcaga	858
															atctct	918
															ggaaaa	978
	aaat		-			-	-									986

```
<210> 351
```

<220>

<221> CDS

<222> 282..389

<221> sig_peptide <222> 282..332

<223> Von Heijne matrix score 3.5 seq RWWCFHLQAEASA/HP

<221> polyA_signal

<222> 1413...1418

<221> polyA_site

<222> 1437..1447

ataataatat ctaaaaagct aaattttaaa taccagcttt acataaatga ttgtkgactc 60 tggtctgtkt ctgacacctt tccagaaaaa agtcaattgt tcaggtacac caaagaggaa 120

<211> 1447

<212> DNA

<213> Homo sapiens

gaagagetgt ggaggeeace etetacaaag etttatagaa ettetggate taaeteacaa	180
acaagettee agaagagaet agagaeetta ggeeaggaga tgaaggagtt cagtagcaaa	240
gtcacacctg tecaatteee tgagetttge teacteaget a atg gga tgg caa agg	296
	230
Met Gly Trp Gln Arg	
-15	
tgg tgg tgc ttt cat ctt cag gca gaa gcc tct gcc cat ccc cct caa	344
Trp Trp Cys Phe His Leu Gln Ala Glu Ala Ser Ala His Pro Pro Gln	
-10 -5 1	
ggg ctg cag gcc caa ttc tca tgc tgc cct tgg gtg ggc atc tgt	389
Gly Leu Gln Ala Gln Phe Ser Cys Cys Pro Trp Val Gly Ile Cys	
5 10 15	
	440
taacaaadga aaacgtctgg gtggcggcag casctttgct ctgagtgcct acaaagctaa	449
tgcttggtgc tagaaacatc atcattatta aacttcagaa aagcagcagc catgttcagt	509
caggeteatg etgeeteact gettaagtge etgeaggage egeetgeeaa reteceette	569
ctacacctgg cacactgggg tctgcacaag gctttgtcaa ccaaaracag cttcccccww	629
ttgattgcct gtagactttg gagccaaraa acactctgtg tgactctaca cacacttcag	689
gtggtttgtg cttcaaagtc attgatgcaa cttgaaagga aacagtttaa tggtggaaat	749
gaactaccat ttataacttc tgttttttta ttgagaaaat gattcacgaa kkccaratca	809
gattgccagg aagaaatagg acgtgacggt actgggccct gtgattctcc cagcccttgc	869
agtocgotag gtgagaggaa aagotottta ottocgocco tggcagggao ttotgggtta	929
tgggagaaac cagagatggg aatgaggaaa atatgaacta cagcagaagc ccctgggcag	989
ctgtgatgga gcccctgaca ttactcttct tgcatctgtc ctgccttctt tccctctgcg	1049
aggcagtggg gtgggattca gagtgcttag tctgctcact gggagaagaa gagttcctgc	1109
gcatgcaagc cctgctgtgt ggctgtcgtt tacatttggg aggtgtcctg tatgtctgta	1169
cgttggggac tgcctgtatt tggaagattt aaaaacctag catcctgttc tcaccctcta	1229
agctgcattg agaaatgact cgtctctgta tttgtattaa gccttaacac ttttcttaag	1289
tgcattcggt gccaacattt tttagagctg taccaaaaca aaaagcctgt actcacatca	1349
camtgtcatt ttgataggag cgttttgtta tttttacaag gcagaatggg gtgtaacagt	1409
tgaattaaac ttagcaatca cgtgctcaaa aaaaaaaa	1447
<210> 352	
<210> 352 <211> 1641	
<211> 1641	
<211> 1641 <212> DNA	
<211> 1641	
<211> 1641 <212> DNA <213> Homo sapiens	
<211> 1641 <212> DNA <213> Homo sapiens <220>	
<211> 1641 <212> DNA <213> Homo sapiens <220> <221> CDS	
<211> 1641 <212> DNA <213> Homo sapiens <220>	
<211> 1641 <212> DNA <213> Homo sapiens <220> <221> CDS	
<211> 1641 <212> DNA <213> Homo sapiens <220> <221> CDS	
<211> 1641 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 208339 <221> sig_peptide	
<211> 1641 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 208339 <221> sig_peptide <222> 208294	
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339 </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339 </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix score 5.59999990463257</pre>	
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339 </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339 </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339 </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix score 5.59999990463257</pre>	
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339 </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	60
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	60
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208.339  &lt;221&gt; sig_peptide &lt;222&gt; 208.294 &lt;223&gt; Von Heijne matrix</pre>	120
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	120 180
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208.294 &lt;223&gt; Von Heijne matrix</pre>	120
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	120 180
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208.294 &lt;223&gt; Von Heijne matrix</pre>	120 180
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	120 180 234
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	120 180
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	120 180 234
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208.294 &lt;223&gt; Von Heijne matrix</pre>	120 180 234 282
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	120 180 234
<pre>&lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208.294 &lt;223&gt; Von Heijne matrix</pre>	120 180 234 282

```
gaa aag gcg taatgaaaac catcccgtcc ccattcctcc tcctctctqa
                                                                      379
Glu Lys Ala
        15
gggactggag ggaagccgtg cttctgagga acaactctaa ttagtacact tgtgtttgta
                                                                      439
ratttacacw wtgtattatg tattaacatg gcgtgtttat ttttgtattt ttctctggtt
gggagtatka tatgaaggat caarateete aacteacaca tgtaracaaa cattasetet
                                                                      559
ttactettte teaacecett wtatgatttt aataattete acttaactaa ttttgtaage
                                                                      619
ctgagatcaa taagaaatgt tcaggagaga ggaaagaaaa aaaatatatg ctccacaatt
                                                                      679
tatatttaga gagagaacac ttagtcttgc ctgtcaaaaa gtccaacatt tcataggtag
                                                                      739
taggggccac atattacatt cagttgctat aggtccagca actgaacctg ccattacctg
                                                                      799
ggcaaggaaa gatccctttg ctctaggaaa gcttggccca aattgatttt cttcttttc
cccctgtagg actgactgtt ggctaatttt gtcaagcaca gctgtggtgg gaagagttag
ggccagtgtc ttgaaaatca atcaagtagt gaatgtgatc tctttgcara gctatagata
                                                                      979
gaaacagctg gaaaactaaa ggaaaaatac aagtgttttc ggggcataca ttttttttct
                                                                     1039
gggtgtgcat ctgttgaaat gctcaagact taattatttg ccttttqaaa tcactqtaaa
                                                                     1099
tgcccccatc cggttcctct tcttcccarg tgtgccaagg aattaatctt ggtttcacta
                                                                     1159
caattaaaat tcactccttt ccaatcatgt cattgaaagt gcctttaacg aaagaaatgg
                                                                     1219
tcactgaatg ggaattctct taagaaaccc tgagattaaa aaaagactat ttggataact
                                                                     1279
tataggaaag cotagaacot cocagtagag tggggatttt tttcttcttc cotttctct
                                                                     1339
ttggacaata gttaaattag cagtattagt tatgagtttg gttgcagtgt tcttatcttg
                                                                     1399
tgggctgatt tccaaaaacc acatgctgct gaatttacca gggatcctca tacctcacaa
                                                                     1459
tgcaaaccac ttactaccag gcctttttct gtgtccactg gagagettga gctcacactc
aaagatcaga ggacctacag agagggctct ttggtttgag gaccatggct tacctttcct
                                                                     1579
geetttgace cateacacee cattteetee tettteete teecegetge caaaaaaaa
                                                                     1639
aa
                                                                     1641
<210> 353
<211> 884
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 69..557
<221> sig_peptide
<222> 69..224
<223> Von Heijne matrix
      score 4.69999980926514
      seq LGLALGRLEGGSA/RH
<221> polyA_signal
<222> 849..854
<221> polyA_site
<222> 870..883
<400> 353
attggctccg gatcgtqcqt gaggcggctt cgtgggcagc gagaqtcaca gacaagacag
                                                                       60
caageagg atg gag cac tae egg aaa get gge tet gta gag ete eea geg
                                                                      110
         Met Glu His Tyr Arg Lys Ala Gly Ser Val Glu Leu Pro Ala
                 -50
                                      -45
cct tcc cca atg ccc cag cta cct cct gat acc ctt gag atg cgg gtc
                                                                      158
Pro Ser Pro Met Pro Gln Leu Pro Pro Asp Thr Leu Glu Met Arg Val
            -35
                                 -30
cga gat ggc agc aaa att cgc aac ctg ctg ggg ttg gct ctg ggt cgg
Arg Asp Gly Ser Lys Ile Arg Asn Leu Leu Gly Leu Ala Leu Gly Arg
                            -15
                                                 -10
        -20
ttg qaq ggc ggc aqt gct cgg cat gta gtg ttc tca ggt tct ggc agg
                                                                       254
```

Leu Glu Gly Gly Ser Ala Arg His Val Val Phe Ser Gly Ser Gly Arg -5 1 5 10	
gct gca gga aag gct gtc agc tgc gct gag att gtc aag cgg cgg gtc Ala Ala Gly Lys Ala Val Ser Cys Ala Glu Ile Val Lys Arg Arg Val 15 20 25	302.
ccg ggc ctg cac cag ctc acc aag cta ckt ttc ctt caa act gag gac Pro Gly Leu His Gln Leu Thr Lys Leu Xaa Phe Leu Gln Thr Glu Asp 30 35	350
age tgg gte cca see tea cet gae aca ggg eta rac cee etc aca gtg Ser Trp Val Pro Xaa Ser Pro Asp Thr Gly Leu Xaa Pro Leu Thr Val 45	398
cgc cgc cat gtg cct gca ktg tgg gtg ctg ctc asc cgg gac ccc ctg Arg Arg His Val Pro Ala Xaa Trp Val Leu Leu Xaa Arg Asp Pro Leu 60 65 70	446
gac ccc aat gag tgt ggt tac caa ccc cca gga gca ccc cct ggc ctg Asp Pro Asn Glu Cys Gly Tyr Gln Pro Pro Gly Ala Pro Pro Gly Leu 75 80 90	494
ggt tee atg eee age tee age tgt gge eet egt tee era aaa agg get Gly Ser Met Pro Ser Ser Ser Cys Gly Pro Arg Ser Xaa Lys Arg Ala 95 100	542
cra rac acc cga tcg tgaaaacctg ctgasccagc ctgttctccg ggcctraatg Xaa Xaa Thr Arg Ser 110	597
totggggtgc ttgtgccttt totranaagc gttgtgaskg ctcaacatcc ccatcaaggt	657
ttgagtccac aaaagtggac ctccctatca tgcttcccct tccctctagc atgtgggaag	717
ggactgctgt gaagaatgac agatgtgggg cctctgccaa gttctgcatt gctaaataag	7 <b>77</b>
ggetteetet geettetaee tacagtgeat ttgaaetgee ttetgaaaga ggteeakgga gggatttagg aaataaagtt tetaeetatt tgaaaaaaaa aaaacae	837 884
Joseph and Canada Color	001
<210> 354	
<211> 729 <212> DNA <213> Homo sapiens	
<212> DNA <213> Homo sapiens	
<212> DNA	
<212> DNA <213> Homo sapiens <220>	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 134325  <221> sig_peptide <222> 134274 <223> Von Heijne matrix score 5.90000009536743	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 134325  <221> sig_peptide <222> 134274 <223> Von Heijne matrix	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 134325  <221> sig_peptide <222> 134274 <223> Von Heijne matrix score 5.90000009536743	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 134325  &lt;221&gt; sig_peptide &lt;222&gt; 134274 &lt;223&gt; Von Heijne matrix</pre>	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 134325  <221> sig_peptide <222> 134274 <223> Von Heijne matrix	60
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 134325  <221> sig_peptide <222> 134274 <223> Von Heijne matrix	120
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 134325  <221> sig_peptide <222> 134274 <223> Von Heijne matrix	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 134325  &lt;221&gt; sig_peptide &lt;222&gt; 134274 &lt;223&gt; Von Heijne matrix</pre>	120 169
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 134325  &lt;221&gt; sig_peptide &lt;222&gt; 134274 &lt;223&gt; Von Heijne matrix</pre>	120 169
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 134325  &lt;221&gt; sig_peptide &lt;222&gt; 134274 &lt;223&gt; Von Heijne matrix</pre>	120 169 217

WO 99/31236 -270- PCT/IB98/02122

Leu His Cys Phe Pro Asp Leu Pro Thr	
gga ktc aac act tgagcctagg gtgggcta Gly Xaa Asn Thr	10 ca acaaaaratt ctaatttacc 365
ttgcttcatc taggtccagg ccccaaktag ct atttattgta ttgtataasc taaaaacatt ta ascaatcttt tttctgttca cggtgtttgt ga tttttgaaaa aatgggaatt gaccggatag ww tcatttaact tttataaaca tgccttctc ct aagttggatc tatcctcagt aactctgcca tg aaaa	tttttgtt gaatcraaac aattccatgt 485 taaaaacct taaattccgc aagcatcagt 545 acaggcaa agwtataaat agctacaaca 605 attgaara catctgatat ttttgctgga 665
<210> 355 <211> 1013 <212> DNA <213> Homo sapiens	
<220>	
<221> CDS <222> 78731	
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 78227 &lt;223&gt; Von Heijne matrix</pre>	
<221> polyA_site <222> 10021013	
<2225 10021013	
<400> 355	gcacagaa gagtgagaag gaagcgacta 60
<400> 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc Met His His Gly	ctc aca cca ctg tta ctt ggt 110 Leu Thr Pro Leu Leu Gly
<400> 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc	ctc aca cca ctg tta ctt ggt 110 Leu Thr Pro Leu Leu Leu Gly -45 g aaa ttt tta atc aag aaa aaa 158
<pre>&lt;400&gt; 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc</pre>	ctc aca cca ctg tta ctt ggt 110  Leu Thr Pro Leu Leu Leu Gly -45 -40  g aaa ttt tta atc aag aaa aaa 158  Lys Phe Leu Ile Lys Lys Lys -30 -25  c gga aga act gct ctc ata ctt 206  c Gly Arg Thr Ala Leu Ile Leu
<pre>&lt;400&gt; 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc</pre>	ctc aca cca ctg tta ctt ggt Leu Thr Pro Leu Leu Leu Gly -45 g aaa ttt tta atc aag aaa aaa 158 Lys Phe Leu Ile Lys Lys Lys -30 cgga aga act gct ctc ata ctt 206 c Gly Arg Thr Ala Leu Ile Leu -10 a gtc agc ctt cta ctt gag caa 254 c Val Ser Leu Leu Leu Glu Gln
<pre>&lt;400&gt; 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc</pre>	ctc aca cca ctg tta ctt ggt Leu Thr Pro Leu Leu Leu Gly -45 g aaa ttt tta atc aag aaa aaa Lys Phe Leu Ile Lys Lys Lys -30 c gga aga act gct ctc ata ctt Gly Arg Thr Ala Leu Ile Leu -10 g gtc agc ctt cta ctt gag caa val Ser Leu Leu Leu Glu Gln 5 g tct gga cag acg gcc aaa aag ser Gly Gln Thr Ala Lys Lys
<pre>&lt;400&gt; 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc</pre>	ctc aca cca ctg tta ctt ggt Leu Thr Pro Leu Leu Leu Gly -45 g aaa ttt tta atc aag aaa aaa 158 Lys Phe Leu Ile Lys Lys Lys -30 gga aga act gct ctc ata ctt 206 Gly Arg Thr Ala Leu Ile Leu -10 g gtc agc ctt cta ctt gag caa 254 g Val Ser Leu Leu Glu Gln 5 g tct gga cag acg gcc aaa aag 302 g Ser Gly Gln Thr Ala Lys Lys 20 g att tgc cag tta ctt tct gac 350
<pre>&lt;400&gt; 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc</pre>	ctc aca cca ctg tta ctt ggt Leu Thr Pro Leu Leu Leu Gly -45 -40 g aaa ttt tta atc aag aaa aaa 158 Lys Phe Leu Ile Lys Lys Lys -30 -25 gga aga act gct ctc ata ctt 206 g Gly Arg Thr Ala Leu Ile Leu -10 g gtc agc ctt cta ctt gag caa 254 g Val Ser Leu Leu Leu Glu Gln 5 g tct gga cag acg gcc aaa aag 302 g Ser Gly Gln Thr Ala Lys Lys 20 a att tgc cag tta ctt tct gac 350 g Ile Cys Gln Leu Leu Ser Asp 35
<pre>&lt;400&gt; 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc</pre>	ctc aca cca ctg tta ctt ggt Leu Thr Pro Leu Leu Leu Gly -45 -40 g aaa ttt tta atc aag aaa aaa 158 Lys Phe Leu Ile Lys Lys Lys -30 -25 gga aga act gct ctc ata ctt 206 g Gly Arg Thr Ala Leu Ile Leu -10 g gtc agc ctt cta ctt gag caa 254 g Val Ser Leu Leu Leu Glu Gln 5 g tct gga cag acg gcc aaa aag 302 g Ser Gly Gln Thr Ala Lys Lys 20 a att tgc cag tta ctt tct gac 350 g Ile Cys Gln Leu Leu Ser Asp 35 c tct tct gaa aac agc aat cca 398
<pre>&lt;400&gt; 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc</pre>	ctc aca cca ctg tta ctt ggt Leu Thr Pro Leu Leu Leu Gly -45 -40  g aaa ttt tta atc aag aaa aaa 158 Lys Phe Leu Ile Lys Lys Lys -30 -25 gga aga act gct ctc ata ctt Gly Arg Thr Ala Leu Ile Leu -10 gtc agc ctt cta ctt gag caa 254 Val Ser Leu Leu Leu Glu Gln 5 a tct gga cag acg gcc aaa aag 302 Ser Gly Gln Thr Ala Lys Lys 20 25 a att tgc cag tta ctt tct gac 11e Cys Gln Leu Leu Ser Asp 35 c tct tct gaa aac agc aat cca 1 Ser Ser Glu Asn Ser Asn Pro 55 g gaa gag tca caa agg ctt aaa 446
<pre>&lt;400&gt; 355 agtttccaag ggaaggagca gcgtgtggga aa aattttattt actttct atg cat cat ggc</pre>	ctc aca cca ctg tta ctt ggt  Leu Thr Pro Leu Leu Leu Gly -45 -40  g aaa ttt tta atc aag aaa aaa 158  Lys Phe Leu Ile Lys Lys Lys -30 -25  gga aga act gct ctc ata ctt 206  g Gly Arg Thr Ala Leu Ile Leu -10  g gtc agc ctt cta ctt gag caa 254  g Val Ser Leu Leu Leu Glu Gln 5  a tct gga cag acg gcc aaa aag 302  a tct gga cag acg gcc aaa aag 302  a ser Gly Gln Thr Ala Lys Lys 20 25  a att tgc cag tta ctt tct gac 350  a lle Cys Gln Leu Leu Ser Asp 35  c tct tct gaa aac agc aat cca 398  c tct tct gaa aac agc aat cca 398  d Ser Ser Glu Asn Ser Asn Pro 55  g gaa gag tca caa agg ctt aaa 446  d Glu Glu Ser Gln Arg Leu Lys 70  a atg tct caa gaa cca gaa ata 494

aat arg ggt ggt gat aga aag gtt gaa raa raa atg aar aag cac gga Asn Xaa Gly Gly Asp Arg Lys Val Glu Xaa Xaa Met Lys Lys His Gly 90 95 100 105	542
agt wet cat atg gga tte eea raa aac etg met aac ggt gee act get Ser Xaa His Met Gly Phe Pro Xaa Asn Leu Xaa Asn Gly Ala Thr Ala 110 115 120	590
gac aat ggt gat gat gga tta att ccm cca rgg aaa asc ara aca cct Asp Asn Gly Asp Asp Gly Leu Ile Pro Pro Xaa Lys Xaa Xaa Thr Pro 125 130 135	638
gaa agc cas caa ttt cct gac act gag aat gaa cag tat cac agg gac Glu Ser Xaa Gln Phe Pro Asp Thr Glu Asn Glu Gln Tyr His Arg Asp 140 145 150	686
ttt tct ggc cat ccc mac ttt ccc acd acc ctt ccc atc aaa cag Phe Ser Gly His Pro Xaa Phe Pro Thr Thr Leu Pro Ile Lys Gln 155 160 165	731
tgatgaacaa aatgatacto hsaagommot ttotgaagam caraacactg gaatattaca	791
agatgagatt ctgattcatg aagaaaagca gatagaagtg gctgaaaatg aattctgagc	851
tttctcttag ttataaraaa gaaaaagacc tcttgcatga aaatagtacg ttgcaggaag	911
aaattgtcat gctaaractg gaactagack taatgaaaca tcagagccag ctaararaaa	971
araaatattt ggaggaaatt gaaagtgtgg aaaaaaaaa	1013
<pre>&lt;210&gt; 356 &lt;211&gt; 973 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 46693  &lt;221&gt; sig_peptide &lt;222&gt; 4690 &lt;223&gt; Von Heijne matrix</pre>	<b>5</b> 7
aageggetgg teeceggaag ttggaegeat gegeegttte tetge atg gtg tge gtt Met Val Cys Val -15	57
ctc gtt cta gct gcg gcc gca gga gct gtg gcg gtt ttc cta atc ctg Leu Val Leu Ala Ala Ala Ala Gly Ala Val Ala Val Phe Leu Ile Leu -10 -5 1 5	105
cga ata tgg gta gtg ctt cgt tcc atg gac gtt acg ccc cgg gag tct Arg Ile Trp Val Val Leu Arg Ser Met Asp Val Thr Pro Arg Glu Ser 10 15 20	153
ctc agt atc ttg gta gtg gct ggg tcc ggt ggg cat acc act gag atc Leu Ser Ile Leu Val Val Ala Gly Ser Gly Gly His Thr Thr Glu Ile 25 30 35	201
ctg agg ctg ctt ggg agc ttg tcc aat gcc tac tca cct aga cat tat	249
Leu Arg Leu Leu Gly Ser Leu Ser Asn Ala Tyr Ser Pro Arg His Tyr 40 45 50	

gtc att gct gac act gat gaa atg agt gcc aat aaa ata aat tct ttt Val Ile Ala Asp Thr Asp Glu Met Ser Ala Asn Lys Ile Asn Ser Phe

40

297

	55					60					65					
gaa	cta	rat	cga	gsk	gat		rac	cct	aqt	aac		twt	acc	aaa	tac	345
Glu 70	Leu	Xaa	Arg	Xaa	Asp	Arg	Xaa	Pro	Ser	Asn 80	Met	Xaa	Thr	Lys	Tyr 85	313
tac	att	cac	cqa	att		ara	age	caa	σaσ		cag	cag	too	tgg		393
Tyr	Ile	His	Arg	Ile 90	Pro	Xaa	Ser	Arg	Glu 95	Val	Gln	Gln	Ser	Trp	Pro	373
tcc	acc	gtt	tyc	acc	acc	ttg	cac	tcc	atg	tgg	ctc	tcc	ttk	ccc	cta	441
Ser	Thr	Val	Xaa 105	Thr	Thr	Leu	His	Ser 110	Met	Trp	Leu	Ser	Xaa 115	Pro	Leu	
att	cac	agg	gtg	aag	cca	rat	ttg	gtg	ttg	tgt	aac	gga	cca	gga	aca	489
		120					125					130		Gly		
tgt	gty	CCT	atc	tgt	gta	tct	gcc	ctt	ctc	ctt	999	ata	cta	gga	ata	537
	135					140					145			ĞÎy		
aag	aaa	gtg	atc	att	gtc	tac	gtt	gaa	agc	atc	tgc	cgt	gta	aaa	acs	585
	Lys	Val	Ile	Ile		Tyr	Val	Glu	Ser		Cys	Arg	Val	Lys		
150	t c c	2 + 4	+	~~~	155	- <del></del>				160					165	<b>633</b>
Leu	Ser	Met	Ser	Glv	Lvs	Tle	Leu	Dhe	Vie Vie	Len	Ser	aat Aen	Tyr	ttc Phe	att	633
				170	2,0				175	acu.	561	7311	1 y 1	180	116	
gtt	cag	tgg	ccg	gct	ctg	aaa	gaa	aag		ccc	aaa	tcg	gtg		ctt	681
Val	Gln	Trp	Pro	Ala	Leu	Lys	Glu	Lys	Tyr	Pro	Lys	Ser	Val	Tyr	Leu	
			185					190					195			
gly 9 <b>9</b> 9	Arg	Ile		tgac	aaat	gg o	aact	gact	t ct	ttag	gaatt	ttg	cast	taa		733
cact		200														
															gegtet gaara	793 853
				Lalu	id ata	ıcaaa	ıcatt	: aat	:aaac	:gta	acta	CVA	at c	3ttt:	stacct	913
															atgcct aaaaa	913 973
															atgcct aaaaaa	
<210	aaac > 35	са <i>а</i> 7														
<210 <211	aaac > 35 > 86	ca a 7 8														
<210 <211 <212	aaac > 35 > 86 > DN	са а 7 8 А	attt	ctt												
<210 <211	aaac > 35 > 86 > DN	са а 7 8 А	attt	ctt												
<210 <211 <212 <213	aaac > 35 > 86 > DN > Ho	ca a 7 8 A mo s	attt	ctt												
<210 <211 <212 <213 <220 <221	* 35 * 86 * DN * Ho * CD	ca a 7 8 A mo s	apie	ctt												
<210 <211 <212 <213 <220 <221 <222	> 35 > 86 > DN > Ho > CD	7 8 A mo s 65	apie	ens												
<210 <211 <212 <213 <220 <221 <222 <221	* 35	ca a 7 8 A mo s 6s	apie	ens												
<210 <211 <212 <213 <220 <221 <222 <221 <222	35 > 35 > 86 > DN > Ho > CD > 12 > si > 12	7 8 A mo s 65 g_pe 61	apie	ens le	t ct											
<210 <211 <212 <213 <220 <221 <222 <221	35 > 86 > DN > Ho > CD > 12 > si > 12 > Vo	7 8 A mo s 6 5 g_pe 6 1 n He	apie 27 ptid 82 ijne	ens ens	rix	carat	. <b>.</b>									
<210 <211 <212 <213 <220 <221 <222 <221 <222	35 > 86 > DN > Ho > CD > 12 > si > Vo sc	7 8 A mo s 6 5 g_pe 6 1 n He ore	apie  27  ptid 82  ijne 3.90	ens	rix	6743	. <b>.</b>									
<210 <211 <212 <213 <220 <221 <222 <221 <222	35 > 86 > DN > Ho > CD > 12 > si > Vo sc	7 8 A mo s 6 5 g_pe 6 1 n He ore	apie  27  ptid 82  ijne 3.90	ens	rix	6743	. <b>.</b>									
<210 <211 <212 <213 <220 <221 <222 <221 <222 <223	aaac  > 35 > 86 > DN > HO > CD > 12 > 12 > si > 2 > yoo	7 8 A mo s S 6 5 pe 6 1 n ore IL lyA_	apie 27 ptid 82 ijne 3.90 FHGV	ens emat	rix	6743	. <b>.</b>									
<210 <211 <212 <213 <220 <221 <222 <221 <222	aaac  > 35 > 86 > DN > HO > CD > 12 > 12 > si > 2 > yoo	7 8 A mo s S 6 5 pe 6 1 n ore IL lyA_	apie 27 ptid 82 ijne 3.90 FHGV	ens emat	rix	6743	. <b>.</b>									
<210 <211 <212 <213 <220 <221 <222 <221 <222 <223	aaac  > 35 > 86 > DN + O  > CD + Si	7 8 A mo s S 6 5 Pe 6 1 lyA_ 1 lyA_ 1 lyA_ 1	apie 27 ptid 82 ijne 3.90 FHGV sign 3.9	ens mat 00000 FYAG	rix	6743	. <b>.</b>									
<210 <211 <212 <213 <220 <221 <222 <221 <222 <221 <222 <221 <222 <221	aaac  > 35 > 86 > DN + O  > CD + Si	7 8 A mo s S 6 5 Pe 6 1 lyA_ 1 lyA_ 1 lyA_ 1	apie 27 ptid 82 ijne 3.90 FHGV sign 3.9	ens mat 00000 FYAG	rix	6743	. <b>.</b>									
<210 <211 <212 <213 <220 <221 <222 <221 <222 <221 <222 <400	aaac	7 8 A mo s S 6 5 pe 6 1 ly A _ 8 ly A _ 8 ly A _ 7	apie 27 ptid 82 ijne 3.90 sign 3.9 site 67	ens FYAG	rix 0953 GFA/	6743		a ata	etgta	atta	ctad	cctgo	caa a	aaaa	aaaaaa	973
<210 <211 <212 <213 <220 <221 <222 <221 <222 <221 <222 <400 actg	aaac	7 8 A mo S 6 5 per 6 n re IL 1 y A 8 1 y A 8 7 aa c	apie 27 ptid 82 ijne 3.90 FHGV sign 3.9 tcgt	ens mat	rix 0953 GGFA/	6743	gtago	: gtg	etgta	ntta	ctad	cctgo	cac .	agga	caactt	973
<210 <211 <212 <213 <220 <221 <222 <221 <222 <221 <222 <400 actg gcct	aaac	7 8 A m S 6 9 1.1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	apie 27 ptid 82 ijne 3.90 FHGV sign 3.9 tcgt	ens mate of the control of the contr	rix 00953 GGFA/	36743	gtago	e gtg	ggtgo gatg	etta	:gt	cgct	cac .	agga ggaa	caactt	973 60 120
<210 <211 <212 <213 <220 <221 <222 <221 <222 <221 <222 <400 actg gcct	aaac	Ca a a 7 8 Am S 6 9 1 9 6 7 aa g C C C C C C C C C C C C C C C C C	apie 27 ptid 82 ijne 3.90 FHGV sign 3.9 tctttt	ens e mate of	rix 10953 GGFA/	ettte	gtage	e gtg	ggtgo gatgo	etta eggc	tgt: aaac	cgct gtat	cac :	agga ggaa tc t	caactt gcaggc at gcc	973
<210 <211 <212 <213 <220 <221 <222 <221 <222 <221 <222 <400 actg gcct	aaac	Ca a a 7 8 Am S 6 9 1 9 6 7 aa g C C C C C C C C C C C C C C C C C	apie 27 ptid 82 ijne 3.90 FHGV sign 3.9 tctttt	ens e mate of	rix 10953 GGFA/	ettte	gtage	e gtg	ggtgo gatgo	ette 1990 100 c. c.	tgt: aaac	cgct gtat	cac :	agga ggaa tc t	caactt	973 60 120

Gly 999	ggc Gly	ttt Phe	gcc Ala	att Ile 1	gtg Val	tat Tyr	tac Tyr	ctc Leu 5	att Ile	caa Gln	aag Lys	ttt Phe	cat His 10	tcc Ser	agg Arg	218
			tac Tyr													266
			gct Ala									tat				314
atc Ile 45	gac Asp	agg Arg	gaa Glu	aac Asn	ttc Phe 50	gtg Val	gac Asp	att Ile	gtt Val	rat Xaa 55	gcc Ala	aag Lys	ttg Leu	aaa Lys	att Ile 60	362
			gga Gly													410
			Pro 80													458
			ggt Gly													506
			gtg Val				taga	agac	gac o	caga	aagao	ec e	gcti	tgcti	ŧ.	557
													_		tcagtg	617
-			_				_		_		_				cagcac	677
								-	_	-	_		-		ttaaac	737
															gtgctt	797
_		iaa a	_	acga	ic aa	aaagg	gaaco	e aga	lacta	aca	aaaı	gtt	gt	cgac	ctttaa	857 868
<211 <212	> 35 > 51 > DN > Ho	.9 IA	sapie	ns												
<220																
	.> CI															
<222	> 66	532	20													
<222	:> 66 :> Vo so	n He ore	≘ijn∈	e mat		/vr										
	-	01yA 00	_sigr 495	nal												
	-	olyA_ 089	_site 519	2												
<400	> 39	58														
			taaco	casa	ag a	ctqc	ttqc	t qc	ggca	gaca	cqc	caqa	kgt	gcac	gctccag	6
	a at	g go	ca gt	ga	eg g	cg t	tg g eu A	cg g	cg m	rg a	cg t	gg c	tt g	gc g	tg tgg	110
ggc	gta	agg	acc	atq	caa	gcc	cga	ggc	ttc	ggo	tcg	gat	cag	g tcc	gag	15
															Glu 15	

WO 99/31236 -274 - PCT/IB98/02122

aat gtc gac egg ggc ggg ggc tcc atc egg gaa gcc ggt ggg gcc ttc Asn Val Asp Arg Cly Ala Cly Ser ILe Arg Clu Ala Cly Cly Ala Phe Arg Ala Gly Ala Cly Ser ILe Arg Clu Ala Cly Cly Ala Phe  gga aag aga gag cag gct gaa gag gas ega tat ttc ega gac cag agt Cly Lys Arg Clu Clu Ala Clu Clu Clu Arg Tyr Phe Arg Ala Cln Ser  aca gaa caa ctg gca rct ttg aaa aaa crc cat gaa gaa gar atc gtt Thr Glu Cln Leu Ala Xaa Leu Lys Lys Xaa His Clu		
Color   Colo	Asn Val Asp Arg Gly Ala Gly Ser Ile Arg Glu Ala Gly Gly Ala Phe	206
The Glu Gln Leu Ala Xaa Leu Lys Lys Xaa His Glu Glu Glu Tle Val  50 55 56 Cat cat aga gaa gga ttgagcgtctg cagaaagaaa ttgagcgcca  His His Arg Glu Gly Asp 65 taagcagaag atcaaaatgc tagaacatga tgattaagtg cacaccgtgt gccatagaat ggcacatgtc attgcccact tctgtgtaaa catggttctg gtttaactaa tatttgtctg tgtgctacta acagattata ataaattgtc atcagtgaaa aaaaaaaaa  410 ggcacatgtc attgcccact tctgtgtaaa catggttctg gtttaactaa tatttgtctg tgtgctacta acagattata ataaattgtc atcagtgaaa aaaaaaaaa  519  <2210 359 <2211 1028 <2212 DNA  <2213 Homo sapiens  <2220 2211 CDS <2222 731.948  <2213 Von Heijne matrix score 4.40000009536743 seq IVLHLVLQGMVYT/EY  <2213 PolyA_site <2221 polyA_site <2222 10161028  <400 359 acc at gc at g at g ctt cat tac ctt ttc cat acg aga acc Met His Gly Leu Leu His Tyr Leu Phe His Thr Arg Asn -25 cac acc ttc att gtc ctg cac ctg gtc ttg caa ggg atg gtt tat act His Thr Phe Tle Val Leu His Leu Val Leu'Oln Gly Met Val Tyr Thr -15 -10 -25 aga tac acc tgg gaa gta ttt gcg tac tgt cag gag ttg tcc Glu Tyr Thr Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu Ser 1 5 10 15 ttg cat tac ctt ctt ctg ccc tat ctg ctg cta gg gta aac ctg ttt Leu His Tyr Leu Leu Phe Tyr Leu Leu Leu Qla Asn Leu Phe 20 ttt tac ccc ttg act tgg acc aat cct gga att ata aca aaa gca The Phe Thr Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys Ala 35 at gaa tat tta tt ctt cat gtt tag at tta ag gaa ktg attt Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe 50 cca aac act gg akt gtg tac tct tt gat tta ag aaa cca gct cga 1399 Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg 65 cra aas cac tgc akt gtg tgt aac tgg tgt cac cgt ttc rac cat 447	Gly Lys Arg Glu Gln Ala Glu Glu Glu Arg Tyr Phe Arg Ala Gln Ser	254
His His Arg Glu Gly Asp 65  taagcagaag atcaaaatgc tagaacatga tgattaagtg cacaccgtg gccatagaat ggcacatgtc attgcccart tctgtgtaaa catggttctg gtttaactaa tatttgtctg 470 tgtgccactact acagattata ataaattgtc atcagtgaaa aaaaaaaaa 519  <210	Thr Glu Gln Leu Ala Xaa Leu Lys Lys Xaa His Glu Glu Glu Ile Val	302
taagcagaag atcaaaatgc tagaacatga tgattaagtg cacaccgtgt gccatagaat ggcaatgtc attgccact tctgtgtaaa catggttctg gtttaactaa tatttgtctg 470 470 470 470 470 470 470 470 470 470	His His Arg Glu Gly Asp	350
<pre>&lt;211&gt; 1028 &lt;212&gt; DNA &lt;2213 Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 73948 </pre> <pre>&lt;221 sig_peptide &lt;222&gt; 73159 &lt;223&gt; Von Heijne matrix</pre>	taagcagaag atcaaaatgo tagaacatga tgattaagtg cacaccgtgt gccatagaat ggcacatgto attgcccact totgtgtaaa catggttotg gtttaactaa tatttgtotg	470
<pre>&lt;211&gt; 1028 &lt;212&gt; DNA &lt;2213 Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 73948 </pre> <pre>&lt;221 sig_peptide &lt;222&gt; 73159 &lt;223&gt; Von Heijne matrix</pre>	2210× 359	
<pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 73948  </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 73159 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>	<211> 1028 <212> DNA	
<pre> &lt;221&gt; CDS &lt;222&gt; 73948  </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 73159 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 73159 &lt;223&gt; Von Heijne matrix     score 4.4000009536743     seq IVLHLVLQGMVYT/EY  &lt;221&gt; polyA_site &lt;222&gt; 10161028  </pre> <pre>&lt;400&gt; 359     agctttaaag gcctggccag gggaggagca cagatattt cctgtataat tccagaatgt</pre>	<221> CDS	
<pre>&lt;223&gt; Von Heijne matrix</pre>	<221> sig_peptide	
<pre><dustriance< td=""><td>&lt;223&gt; Von Heijne matrix score 4.40000009536743</td><td></td></dustriance<></pre>	<223> Von Heijne matrix score 4.40000009536743	
agctttaaag gcctggccag gggaggagca cagatatttt cctgtataat tccagaatgt cttcagagag cc atg cat gga ttg ctt cat tac ctt ttc cat acg aga aac Met His Gly Leu Leu His Tyr Leu Phe His Thr Arg Asn -25 -20  cac acc ttc att gtc ctg cac ctg gtc ttg caa ggg gtt tat act 159  His Thr Phe Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr Thr -15 -10 -5  gag tac acc tgg gaa gta ttt ggc tac tgt cag gag ctg gag ttg tcc 207  Glu Tyr Thr Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu Ser 1 15  ttg cat tac ctt ctt ctg ccc tat ctg ctg cta ggt gta aac ctg ttt 255  Leu His Tyr Leu Leu Leu Pro Tyr Leu Leu Leu Gly Val Asn Leu Phe 20 25 30  ttt ttc acc ctg act tgt gga acc aat cct ggc att ata aca aaa gca 303  Phe Phe Thr Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys Ala 35 40 45  aat gaa tta tta ttt ctt cat gtt tat gaa ttt gat gaa ktg atg ttt Asn Glu Leu Leu Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe 50 55 60  cca aaa aac gtg agg tgc tact ctg tgt gat tac agg aaa cca gct cga 399  Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg 65 70 75 80  tcc aas cac tgc akt gtg tgt aac tgg tgt gtg cac cgt ttc rac cat 447  Ser Xaa His Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His		
His Thr Phe Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr Thr  -15  gag tac acc tgg gaa gta ttt ggc tac tgt cag gag ctg gag ttg tcc  Glu Tyr Thr Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu Ser  1	agetttaaag geetggeeag gggaggagea cagatatttt cetgtataat tecagaatgt etteagagag ee atg eat gga ttg ett eat tae ett tte eat aeg aga aac Met His Gly Leu Leu His Tyr Leu Phe His Thr Arg Asn	
gag tac acc tgg gaa gta ttt ggc tac tgt cag gag ctg gag ttg tcc Glu Tyr Thr Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu Ser  1	His Thr Phe Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr Thr	159
ttg cat tac ctt ctt ctg ccc tat ctg ctg cta ggt gta aac ctg ttt  Leu His Tyr Leu Leu Leu Pro Tyr Leu Leu Cly Val Asn Leu Phe  20  25  30  ttt ttc acc ctg act tgt gga acc aat cct ggc att ata aca aaa gca  Phe Phe Thr Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys Ala  35  40  45  aat gaa tta tta ttt ctt cat gtt tat gaa ttt gat gaa ktg atg ttt  Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe  50  55  60  cca aaa aac gtg agg tgc tct act tgt gat tta agg aaa cca gct cga  Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg  65  70  75  80  tcc aas cac tgc akt gtg tgt aac tgg tgt gtg cac cgt ttc rac cat  Ser Xaa His Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His	gag tac acc tgg gaa gta ttt ggc tac tgt cag gag ctg gag ttg tcc Glu Tyr Thr Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu Ser	207
Phe Phe Thr Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys Ala  35  aat gaa tta tta ttt ctt cat gtt tat gaa ttt gat gaa ktg atg ttt  Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe  50  cca aaa aac gtg agg tgc tct act tgt gat tta agg aaa cca gct cga  Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg  65  70  75  80  tcc aas cac tgc akt gtg tgt aac tgg tgt gtg cac cgt ttc rac cat  Ser Xaa His Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His	ttg cat tac ctt ctt ctg ccc tat ctg ctg cta ggt gta aac ctg ttt Leu His Tyr Leu Leu Pro Tyr Leu Leu Leu Gly Val Asn Leu Phe	255
aat gaa tta tta ttt ctt cat gtt tat gaa ttt gat gaa ktg atg ttt  Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe  50	ttt ttc acc ctg act tgt gga acc aat cct ggc att ata aca aaa gca Phe Phe Thr Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys Ala	303
CCa aaa aac gtg agg tgc tct act tgt gat tta agg aaa cca gct cga  Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg  55 70 75 80  tcc aas cac tgc akt gtg tgt aac tgg tgt gtg cac cgt ttc rac cat  Ser Xaa His Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His	aat gaa tta tta ttt ctt cat gtt tat gaa ttt gat gaa ktg atg ttt Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe	351
tcc aas cac tgc akt gtg tgt aac tgg tgt gtg cac cgt ttc rac cat  Ser Xaa His Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His	cca aaa aac gtg agg tgc tct act tgt gat tta agg aaa cca gct cga Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg	399
	tcc aas cac tgc akt gtg tgt aac tgg tgt gtg cac cgt ttc rac cat Ser Xaa His Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His	447

	tgt	_					•			-						495
His	Суѕ	Val	-	Val	Asn	Asn	Cys		Gly	Ala	Trp	Asn		Arg	Xaa	
			100					105					110			_
	ctc			_	_		_	_	_	-	-	-		-	_	543
Phe	Leu		Tyr	Val	Leu	Thr		Thr	Ala	Ser	Ala		Thr	Val	Ala	
		115					120					125				
	gtg															591
Ile	Val	Ser	Thr	Thr	Phe		Val	His	Leu	Val		Met	Ser	Asp	Leu	
	130					135					140					
	cag															639
	Gln	Glu	Thr	Tyr		Asp	Asp	Leu	Gly		Leu	His	Val	Met		
145					150					155					160	
_	gtc				_		-		_						-	687
Thr	Val	Phe	Leu		Gln	Tyr	Leu	Phe		Thr	Phe	Pro	Arg		Val	
				165	•				170					175		
	atg															735
Phe	Met	Leu		Phe	Val	Val	Val		Xaa	Phe	Leu	Leu		Gly	Tyr	
			180					185					190			
	ttg															783
Leu	Leu		Val	Leu	Tyr	Leu		Ala	Thr	Asn	Gln		Thr	Asn	Glu	
		195					200					205				
	tac															831
Trp	Tyr	Arg	Xaa	Asp	Trp	Ala	Trp	Сув	Gln	Arg	•	Pro	Leu	Val	Ala	
	210					215					220					
	cct	_		-	-			_							_	879
_	Pro	Pro	Ser	Ala		Pro	Gln	Val	His	_	Asn	Ile	His	Ser		
225					230					235					240	
	ctt															927
Gly	Leu	Arg	Xaa		Leu	Gln	Glu	Ile		Leu	Pro	Ala	Phe			
				245					250					255		
cat	gag	agg	aag	aaa	caa	gaa	tga	cmag	tgt	atga	ctgc	ct t	tgag	ctgt	a	978
His	Glu	Arg	Lys	Lys	Gln	Glu										
			260													
gtt	cccg	ttt a	attt	acac	at g	tgga	tcct	c gt	tttc	caaa	aaa	aaaa	aaa			1028

<210> 360

<211> 452

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 69..434

<221> sig_peptide

<222> 69..236

<223> Von Heijne matrix score 4.90000009536743 seq FACVPGASPTTLA/FP

<221> polyA_signal

<222> 419..424

<221> polyA_site

<222> 441..452

<400> 360

acagogtgas togocogoca gaagaatatg aaaaagcaga goganotogg ttaagggaaa gegeegag atg acg gge ttt etg etg eeg eee gea age aga ggg aet egg 110 Met Thr Gly Phe Leu Leu Pro Pro Ala Ser Arg Gly Thr Arg

60

-55 -50 -45	
aga tca tgc agc aga agc aga aaa agg caa acg aga aga	158
Arg Ser Cys Ser Arg Ser Arg Lys Arg Gln Thr Arg Arg Arg Arg Asn	
-40 -35 -30	
cca agt age tit gig get teg tgt eea ace ete tig eee tie gee igt	206
Pro Ser Ser Phe Val Ala Ser Cys Pro Thr Leu Leu Pro Phe Ala Cys	'
-25 -20 -15	
gtg eet gga gee agt eee aee aeg ete geg ttt eet eet gta ktg ete	254
Val Pro Gly Ala Ser Pro Thr Thr Leu Ala Phe Pro Pro Val Xaa Leu	
-10 -5 1 5	
aca ggt ccc avc acc gat ggc att ccc ttt gcc ctr nak tct gca gcg	302
Thr Gly Pro Xaa Thr Asp Gly Ile Pro Phe Ala Leu Xaa Ser Ala Ala	
10 15 20	
ggt ccc tit tgt gct tee tte ccc tea ggt ave ete tet ccc cet ggg	350
Gly Pro Phe Cys Ala Ser Phe Pro Ser Gly Xaa Leu Ser Pro Pro Gly	• • •
25 30 35	
cca ctc ccg ggg gtg agg ggg tta ccc ctt ccc agt gtt ttt tat tcc	398
Pro Leu Pro Gly Val Arg Gly Leu Pro Leu Pro Ser Val Phe Tyr Ser	330
••	
tgt ggg gct cac ccc aaa gta tta aaa gta gct ttg taattcaaaa	444
Cys Gly Ala His Pro Lys Val Leu Lys Val Ala Leu	
55 60 65	
aaaaaaa	452
<210> 361	
<211> 875	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 628804	
<222> 628804	
<221> sig_peptide	
<221> sig_peptide <222> 628711	
<221> sig_peptide <222> 628711 <223> Von Heijne matrix	
<221> sig_peptide <222> 628711 <223> Von Heijne matrix score 4.19999980926514	
<221> sig_peptide <222> 628711 <223> Von Heijne matrix	
<221> sig_peptide <222> 628711 <223> Von Heijne matrix score 4.19999980926514 seq_LMPVIPALQEAXA/GG	
<221> sig_peptide <222> 628711 <223> Von Heijne matrix	
<221> sig_peptide <222> 628711 <223> Von Heijne matrix score 4.19999980926514 seq_LMPVIPALQEAXA/GG	
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	60
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480 540
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480 540 600
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480 540
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480 540 600
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480 540 600 654
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480 540 600
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480 540 600 654
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480 540 600 654
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 628711 &lt;223&gt; Von Heijne matrix</pre>	120 180 240 300 360 420 480 540 600 654

aca atg gag act gag gaa gaa ttg ctt aaa cocc agg agg cgg agg Asn Met Glu Thr Glu Ala Gly Glu Leu Leu Lys Pro Arg Arg Arg Arg 15 20 25 ttg car tgaactgaga tcgcaccact gcactccagc ttgggcaaca gagcaagact Leu Gln 30 ttgtctcgca aaaaaaaaaa a 875  <210> 362 <221> 531 <212> DNA <213> Homo sapiens <222> 70108 <222> 70108 <222> 70108 <222> Von Heijne matrix score 3.5 seq MHLLSNWANPASS/RR  <221> polyA signal <222> 496501  <221> polyA signal <222> 521531  <400> 362 aagtggcat ggcggataca gggactacag catcggcgg ggcggctagt gccgctagcg cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg het His Leu Leu Ser Asn Trp Ile Ser Ser Thr Leu 5 10 gca cac tct ttg tca ctg aga gac ttct ttg gat at cat tcg acc ctc Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu 5 10 gca cac tcttt ttg tca ctg aga gac gtc tca gag agg ttg cag ttgc agc 159 Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys 20 25 10 10 10 10 10 10 10 10 10 10 10 10 10		
aac atg gag act gag gaa gag attg ctt aaa ccc agg agg cgg agg 798 Asn Met Glu Thr Glu Ala Gly Glu Leu Leu Lys Pro Arg Arg Arg Arg 15 20 25 ttg car tgaactgaga tegeaceact geactecage ttgggeaaca gagcaagact Leu Gln 30 ttgtetegea aaaaaaaaaa a 875 <pre> &lt;210 &gt; 362 &lt;2211 &gt; 531 &lt;212 &gt; DNA &lt;2213 &gt; Homo sapiens </pre> <pre> &lt;220 &gt; &lt;221 &gt; CDS &lt;222 &gt; 70 366 </pre> <pre> &lt;221 &gt; sig_peptide &lt;222 &gt; 70 108 </pre> <pre> &lt;222 &gt; 70 108 </pre> <pre> &lt;221 &gt; polyA_signal &lt;222 &gt; seq MHLLSNWANPASS/RR </pre> <pre> &lt;221 &gt; polyA_signal &lt;222 &gt; 521 531 </pre> <pre> &lt;220 &gt; cctcgageg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc age aga Amet His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp 11e Ser Ser Thr Leu 5 gca cac tct ttg tca ctg aga gac gtc tca gag agg ctg tgc age tgc Ala His Ser Leu Ser Leu Arg App Val Ser Glu Arg Leu Cys Ser Cys 30 ttg agg aga ct ata agc atg gag cc ttg aga aga ctg ttg cag ttg 30 ttg agg at ata agc atg gag cc ttg gcg ccg gg gt tac cca atg aac Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr 11e Arg Thr 50 Cca atg aga aga tct tca tgc cat tta gaa ttg crg gt tata ttc ctt Tro Met Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val 11e Phe Leu To To</pre>	Ala Xaa Ala Gly Gly Ser Arg Gly Gln Glu Phe Glu Thr Ser Leu Ala	
ttg car tgaactgaga togeaccact geactccage ttgggcaaca gagcaagact Leu Gln 30  ttgtctcgca aaaaaaaaaa a 875  <210> 362 <2211> 531 <212> DNA <2213> Homo sapiens  <220> <221> CDS <222> 70366  <221> sig_peptide <222> 70108 <221> Von Heijne matrix	aac atg gag act gag gca gga gaa ttg ctt aaa ccc agg agg cgg agg Asn Met Glu Thr Glu Ala Gly Glu Leu Leu Lys Pro Arg Arg Arg	798
<pre>c210</pre>	ttg car tgaactgaga tcgcaccact gcactccagc ttgggcaaca gagcaagact Leu Gln	854
<pre>&lt;211&gt; 531 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 70366 </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 70108 </pre> <pre>&lt;221&gt; Non Heijne matrix</pre>	ttgtctcgca aaaaaaaaa a	875
<pre>&lt;211&gt; 531 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 70366 </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 70108 </pre> <pre>&lt;221&gt; Non Heijne matrix</pre>		
<pre>&lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 70366  &lt;221&gt; sig_peptide &lt;222&gt; 70108 &lt;223&gt; Von Heijne matrix</pre>	<210> 362 <211> 531	
<pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 70366  &lt;221&gt; sig_peptide &lt;222&gt; 70108 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;221&gt; CDS &lt;222&gt; 70366  &lt;221&gt; sig_peptide &lt;222&gt; 70108 &lt;223&gt; Von Heijne matrix</pre>	<213> Homo sapiens	
<pre>&lt;222&gt; 70366  &lt;221&gt; sig_peptide &lt;222&gt; 70108  &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;222&gt; 70108 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;222&gt; 70108 &lt;223&gt; Von Heijne matrix</pre>	<221> siq peptide	
score 3.5 seq MHLLSNWANPASS/RR  <221> polyA_signal <222> 496501  <221> polyA_site <222> 521531  <400> 362 aagtggccat ggcggataca gcgactacag catcggcgc ggcggctagt gccgctagcg cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg -10 -5 1  cgt cct tct atg gcc gct tca ggc act tct tgg ata tca tcg acc ctc Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu 5 10  gca cac tct ttg tca ctg aga gac gtc tca gag agg ctg tgc agc tgc Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys 20 25 10 15 15 16 17 18 19 19 19 19 19 19 19 19 19 19 19 19 19	<222> 70108	
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 496501  &lt;221&gt; polyA_site &lt;222&gt; 521531  &lt;400&gt; 362 aagtggccat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg 60 cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga 111</pre>		
<pre>&lt;221&gt;</pre>	seq MHLLSNWANPASS/RR	
<pre>&lt;221&gt; polyA_site &lt;222&gt; 521531  &lt;400&gt; 362 aagtggccat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg 60 cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga 111</pre>	<221> polyA_signal	
<pre>&lt;222&gt; 521531  &lt;400&gt; 362 aagtggccat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga</pre>	<222> 496501	
<pre>&lt;400&gt; 362 aagtggccat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga</pre>		
aagtggcat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga  Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg  -10 -5 1  cgt cct tct atg gcc gct tca ggc act tct tgg ata tca tcg acc ctc  Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu  5 10 15  gca cac tct ttg tca ctg aga gac gtc tca gag agg ctg tgc agc tgc  Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys  20 25 30  tgg agg act ata agc atg gga ccc tgc gcc cgg ggg tca cca atg aac  Trp Arg Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn  35 40 45  agc tct gga gtg cac aga aaa tca agc agg cta ttc tac atc cgg aca  Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr  50 55 60  cca atg aga aga tct tca tgc cat tta gaa tgt crg gtt ata ttc ctt  Pro Met Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu  70 75 80	<222> 521531	
cetegageg atg cac etc ett tee aac tgg gea aac eec get tee age aga  Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg  -10  -5  1  cgt eet tet atg gee get tea gge act tet tgg ata tea teg ace etc  Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu  5  gea cac tet ttg tea etg aga gac gte tea gag agg etg tge age tge  Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys  20  25  16  17  18  20  20  25  30  19  19  19  19  19  19  19  19  19  1		60
cgt       cct       tct       atg       gcc       gct       tca       ggc       act       tct       tgg       ata       tca       tcg       acc       ctc       159         Arg       Pro       Ser       Met       Ala       Ala       Ser       Gly       Thr       Ser       Trp       Ile       Ser       Ser       Thr       Leu       Leu       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15       16       15       15       15       15       15       15       15       15       15       15       15       15       15       15       15	cetegageg atg cae etc ett tec aac tgg gea aac eec get tee age aga	111
cgt         cct         tct         atg         gcc         gct         tca         ggc         act         tct         tgg         ata         tca         tcg         acc         ctc         159           Arg         Pro         Ser         Met         Ala         Ala         Ser         Gly         Thr         Ser         Trp         Ile         Ser         Ser         Thr         Leu         Leu         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15         15		
gca       cac       tct       ttg       tca       ctg       aga       gac       gtc       tca       gag       agc       tgc       tca       gag       agc       tca       gag       agg       ttg       tgc       agc       tgc       ctg       gag       agg       ctg       tgc       ctg       gag       agg       ctg       ctg       gag       ctg       gag       ctg       ctg       gag       gag       tca       cac       atg       gag       ccc       tgg       ggg       tca       cca       atg       aac       255         Trp       Arg       Thr       Ile       Ser       Met       Gly       Pro       Cys       Ala       Arg       Gly       Ser       Pro       Met       Asn       255         Trp       Arg       Thr       Ile       Ser       Met       Alg       Pro       Cys       Ala       Arg       Gly       Ser       Pro       Met       Asn       255         Trp       Arg       Gly       Val       His       Arg       Leu       Arg       Leu       Phe       Tyr       Ile       Arg       Thr       65         Cca       at	cgt cct tct atg gcc gct tca ggc act tct tgg ata tca tcg acc ctc	159
gca         cac         tct         ttg         cca         ctg         aga         gac         gtc         tca         gag         agg         tgc         tgc         agg         ctg         tgc         agc         tgc         207           tgg         agg         acc         tgc         scc         tgc         ggg         ccc         cgg         ggg         tca         cca         atg         aac         255           Trp         Arg         Thr         Ile         ser         Met         Gly         Pro         Cys         Ala         Arg         Gly         ser         Pro         Met         Asn         255           agc         tct         tgga         gtg         cac         aga         aac         tcys         Ala         Arg         Gly         ser         Pro         Met         Asn         Asn         255           agc         tct         tgga         tgt         cac         aga         aaa         tca         agc         agg         cta         ttc         tac         aga         aaa         tca         agg         cta         ttc         tac         atg         aaa         tca         agg		
20 tgg agg act ata agc atg gga ccc tgc gcc cgg ggg tca cca atg aac Trp Arg Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn 35 agc tct gga gtg cac aga aaa tca agc agg cta ttc tac atc cgg aca Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr 50 cca atg aga aga tct tca tgc cat tta gaa tgt crg gtt ata ttc ctt Pro Met Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu 70 70 75 30 255 40 45 45 66 67 67 68 68 69 69 69 69 69 69 60 60 60 60 60 60 60 60 60 60 60 60 60	gca cac tot ttg toa otg aga gao gto toa gag agg otg tgc ago tgc	207
tgg       agg       act       ata       agg       atg       gga       ccc       tgc       cgg       ggg       tca       cca       atg       aac       255         Trp       Arg       Thr       Ile       Ser       Met       Gly       Pro       Met       Asn       255         agc       tct       gga       gtg       cac       aga       aaa       tca       agg       cta       ttc       tac       acc       303         Ser       Ser       Gly       Val       His       Arg       Lys       Ser       Ser       Arg       Leu       Phe       Tyr       Ile       Arg       Thr         50       55       55       60       65       65         cca       atg       aga       tct       tca       tgc       cat       tta       gaa       tgt       crg       gtt       ata       ttc       ctt       351         Pro       Met       Arg       Ser       Ser       Cys       His       Leu       Glu       Cys       Xaa       Val       Ile       Phe       Leu         Pro       Met       Arg       Ser       Ser       Cys <td></td> <td></td>		
agc tct gga gtg cac aga aaa tca agc agg cta ttc tac atc cgg aca Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr 50 55 60 65 cca atg aga aga tct tca tgc cat tta gaa tgt crg gtt ata ttc ctt Pro Met Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu 70 75 80	tgg agg act ata agc atg gga ccc tgc gcc cgg ggg tca cca atg aac	255
agc tct gga gtg cac aga aaa tca agc agg cta ttc tac atc cgg aca Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr 50 55 60 65  cca atg aga aga tct tca tgc cat tta gaa tgt crg gtt ata ttc ctt Pro Met Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu 70 75 80		
50 55 60 65  cca atg aga aga tct tca tgc cat tta gaa tgt crg gtt ata ttc ctt 351  Pro Met Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu 70 75 80	age tet gga gtg cae aga aaa tea age agg eta tte tae ate egg aca	303
cca atg aga aga tct tca tgc cat tta gaa tgt crg gtt ata ttc ctt  Pro Met Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu  70 75 80	65	
70 75 80	cca atg aga aga tot toa tgo cat tta gaa tgt crg gtt ata tto ott	351
	ttg gga cgc caa ttg taaktgttac cttcaaagga tttccttttc taaaaaatta	406
Leu Gly Arg Gln Leu 85		
ttttaratgt ctaactttat gttattgctc acgggtattt gactgaattg ttgatttagg 466	ttttaratgt ctaactttat gttattgctc acgggtattt gactgaattg ttgatttagg	
ataagtcaat tootggaggg aaattaccaa ataaaatgat atgtatttot taccacaaaa 526 aaaaa		

```
<211> 1244
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 70..366
<221> sig_peptide
<222> 70..108
<223> Von Heijne matrix
      score 3.5
      seq MHLLSNWANPASS/RR
<221> polyA_site
<222> 1233..1244
<400> 363
aagtggccat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg
cetegageg atg cae etc ett tee aac tgg gea aac eec get tee age aga
                                                                     111
         Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg
                      -10
                                          -5
cgt cct tct atg gcc gct tca ggc act tct tgg ata tca tcg acc ctc
Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu
                                10
gca cac tot ttg tca ctg aga gac gtc tca gag agg ctg tgc agc tgc
                                                                     207
Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys
                           25
                                                30
tgg agg act ata agc atg gga ccc tgc gcc cgg ggg tca cca atg aac
                                                                     255
Trp Arg Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn
   35
                        40
                                                                     303
age tet gga gtg cae aga aaa tea age agg eta tte tae ate egg aca
Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr
                    55
                                        60
                                                                      351
cca atg aga aga tot toa tgo cat tta raa tgt cag gtt ata tto ott
Pro Met Arg Arg Ser Ser Cys His Leu Xaa Cys Gln Val Ile Phe Leu
                                                        80
                                                                      406
ttg gga cgc caa ttg tagtcggtct tctcttgccc aaccagacac tggcatccac
Leu Gly Arg Gln Leu
            85
tgtcttctgg cagtggctga accagagcca caatgcctgt gtcaactatg caaaccgcaa
                                                                      466
tgcraccaag cetteacetg catecaagtt catecaggga tacetgggag etgteateag
                                                                      526
cgccgtctcc attgctgtgg gccttatktc ctggttcaga aagccaacaa gttcacccca
                                                                      586
                                                                      646
gecaccegee tteteateca gaggtttgtg cegtteeetg etgtagecag tgccaatate
                                                                      706
tgcaatgtgg tcctgatgcg gtacggggag ctggaggaag ggattgatgt cctggacagc
                                                                      766
gatggcaacc tcgtgggctc ctccaagatc gcagcccgac acgccctgct ggagacggcg
ctgacgcgag tggtcctgcc catgcccatc ctggtgctac ccccgatcgt catgtccatg
                                                                      886
ctggagaaga cggctctcct gcaggcacgc ccccggctgc tectccctgt gcaaagcctc
gtgtgcctgg cagccttcgg cctggccctg ccgctggcca tcagcctctt cccgcaaatg
                                                                     946
tcagagattg aaacatccca attagagccg gagatagccc aggccacgag cagccggaca
                                                                     1006
gtggtgtaca acaaggggtt gtgagtgtgg tcagcggcct ggggacggag cactgtgcag
                                                                     1066
ccggggaget gaggggcarg gccgtagaet cacggctgca cctgcaggga gcagcacgcc
                                                                     1126
aaccccagca gtcctgggcc ccctgggaga gtgctcaacc tacagtggag ggagactgac
                                                                     1186
                                                                     1244
ccattcacat tttaacatag gcaagaggag ttctaacaca tttcgtacaa aaaaaaaa
```

<210> 364

<210> 363

<211> 631

<212> DNA

<213> Homo sapiens

```
<220>
<221> CDS
<222> 111..434
<221> sig_peptide
<222> 111..185
<223> Von Heijne matrix
      score 3.90000009536743
     seq WIAAVTIAAGTAA/IG
<221> polyA_site
<222> 618..631
<400> 364
aatcgcggag tcggtgcttt agtacgccgc tggcaccttt actctcgccg gccgcgcgaa
congtttgag ctoggtated tagtgdacad goottgdaag cgacggdgdd atg agt
                                                                     116
                                                      Met Ser
                                                       - 25
ctg act tcc agt tcc agc gta cga gtt gaa tgg atc gca gca gtt acc
Leu Thr Ser Ser Ser Ser Val Arg Val Glu Trp Ile Ala Ala Val Thr
                                -15
           -20
att get get ggg aca get gea att ggt tat eta get tae aaa aga ttt
                                                                     212
Ile Ala Ala Gly Thr Ala Ala Ile Gly Tyr Leu Ala Tyr Lys Arg Phe
       -5
                           1
tat gtt aaa gat cat cga aat aaa gct atg ata aac ctt cac atc cag
                                                                     260
Tyr Val Lys Asp His Arg Asn Lys Ala Met Ile Asn Leu His Ile Gln
                                        20
                    15
                                                                     308
aaa gac aac ccc aag ata gta cat gct ttt gac atg gag gat ttg gga
Lys Asp Asn Pro Lys Ile Val His Ala Phe Asp Met Glu Asp Leu Gly
                                    35
                30
                                                                     356
gat aaa get gtg tac tge egt tgt tgg agg tee aaa aag tte eea tte
Asp Lys Ala Val Tyr Cys Arg Cys Trp Arg Ser Lys Lys Phe Pro Phe
                                50
                                                                     404
tgt gat ggg gct cac aca aaa cat aac gaa gag act gga gac aat gtg
Cys Asp Gly Ala His Thr Lys His Asn Glu Glu Thr Gly Asp Asn Val
       60
                           65
ggc cct ctg atc atc aag aaa aaa gaa act taaatggaca cttttgatgc
                                                                     454
Gly Pro Leu Ile Ile Lys Lys Lys Glu Thr
                        80
                                                                     514
tgcaaatcag cttgtcgtga agttacctga ttgtttaatt araatgacta ccacctctgt
ctgattcacc ttcgctggat tctaaatgtg gtatattgcm aactgcagct ttcacattta
                                                                     574
tggcatttgt cttgttgaaa catcgtggtg cacatttgtt taaacaaaaa aaaaaaa
<210> 365
```

<211> 781

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 19..567

<221> sig_peptide

<222> 19..63

<223> Von Heijne matrix score 8.39999961853027 seq AMWLLCVALAVLA/WG

<221> polyA_signal

```
<222> 749..754
<221> polyA_site
<222> 771..781
<400> 365
aagtgctgct tacccatc atg gaa gca atg tgg ctc ctg tgt gtg gcg ttg
                                                                      51
                    Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu
                    -15
                                        -10
                                                                      99
gcg gtc ttg gca tgg ggc ttc ctc tgg gtt tgg gac tcc tca.gaa cga
Ala Val Leu Ala Trp Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg
atg aag agt egg gag cag gga aga egg etg gga gee gaa age egg ace
                                                                     147
Met Lys Ser Arg Glu Gln Gly Arg Arg Leu Gly Ala Glu Ser Arg Thr
                            20
                                                25
ctg ctg gtc ata gcg cac cct gac gat gaa gcc atg ttt ttt gct ccc
                                                                     195
Leu Leu Val Ile Ala His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro
                                            40
aca gtg cta ggc ttg gcc cgc cta agg cac tgg gtg tac ctg ctt tgc
                                                                      243
Thr Val Leu Gly Leu Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys
                   50
                                        55
ttc tct gca gga aat tac tac aat caa gga gag act cgt aag aaa gaa
                                                                      291
Phe Ser Ala Gly Asn Tyr Tyr Asn Gln Gly Glu Thr Arg Lys Lys Glu
                65
                                    70
ctt ttg car agc tgt gat gtt ttg ggg att cca ctc tcc agt gta atg
                                                                      339
Leu Leu Gln Ser Cys Asp Val Leu Gly Ile Pro Leu Ser Ser Val Met
                                85
att att gac aac agg gat ttc cca rat gac cca ggc atg cag tgg gac
                                                                      387
Ile Ile Asp Asn Arg Asp Phe Pro Xaa Asp Pro Gly Met Gln Trp Asp
                            100
        95
aca rag cac gtg gcc ara gtc ctc ctt cag cac ata gaa gtg aat ggc
                                                                      435
Thr Xaa His Val Ala Xaa Val Leu Leu Gln His Ile Glu Val Asn Gly
                        115
atc aat ctg gtg gtg act ttc gat gca ggg gga rta agt ggc cac agc
                                                                      483
Ile Asn Leu Val Val Thr Phe Asp Ala Gly Gly Xaa Ser Gly His Ser
                                        135
                    130
aat cac att gct ctg tat gca gct gtg agg aag ctt gag ggc caa att
                                                                      531
Asn His Ile Ala Leu Tyr Ala Ala Val Arg Lys Leu Glu Gly Gln Ile
                                                         155
               145
                                    150
                                                                      577
tgc aag ccc tgt ggc act gga caa gac ttt aag gaa tgagtgctgt
Cys Lys Pro Cys Gly Thr Gly Gln Asp Phe Lys Glu
           160
                                165
                                                                      637
caatcagtgt gcctccacct tcaccatctt cttcccctta ctctcacttc cgtcatgtgt
tttatacaac totcaaatot ttottggaga aggaggatat acatacataa tatgaaatgt
                                                                      697
                                                                      757
gtttgttctt cacagtcacc cgattttact gatatttatt tgcattttac caataaaaag
                                                                      781
aaaatgcaag ctcaaaaaaa aaaa
```

<210> 366

<211> 931

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 19..312

<221> sig_peptide

<222> 19..63

<223> Von Heijne matrix score 8.39999961853027

# seq AMWLLCVALAVLA/WG

<221> polyA_signal <222> 896..901

<221> polyA_site

<222> 921931	
<400> 366	
aagtgotgot taccoato atg gaa goa atg tgg oto otg tgt gtg gog ttg  Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu  -15  -10  -5	51
gcg gtc ttg gca tgg ggc ttc ctc tgg gtt tgg gac tcc tca gaa cga Ala Val Leu Ala Trp Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg	99
atg aag agt cgg gag cag gga rga cgg ctg gga gcc gaa agc cgg acc Met Lys Ser Arg Glu Gln Gly Xaa Arg Leu Gly Ala Glu Ser Arg Thr 15 20 25	147
ctg ctg gtc ata gcg cac cct gac gat gaa gcc atg ttt ttt gct ccc Leu Leu Val Ile Ala His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro 30 35 40	195
aca gtg cta ggc ttg gcc cgc cta agg cac tgg gtg tac ctg ctt tgc Thr Val Leu Gly Leu Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys 45 50 55 60	243
ttc tct gca gtt ttc cgt agg gag cta agt gaa tac acc gaa rgt ctt Phe Ser Ala Val Phe Arg Arg Glu Leu Ser Glu Tyr Thr Glu Xaa Leu 65 70 75	291
acc tct gaa ccc ctc ama gcc tagggacagg arcggccggc ttacctggtg Thr Ser Glu Pro Leu Xaa Ala 80	342
ggttggggga cgtcggcagc tcrcgtacta cgccagcagg attganganc acagaaacag	402
ttgchsttgg ttgtattcag tacctkcatt tccgttggga actccaccwg tacttgttat	462
kctgtggaac tttttttat ttgtagaagg agcaagaata ttgaccttac tatatagcac	522 582
acgaaacaat ctatgctgta tcgtgcctgc tcaatcctta aagttaactt ctaatgatag	642
taaaaracct teetgetgee tttaaaatge agettgtget aktaacatge atgtgteaaa ttgaaraatt agacatagat gactaratar aaagtaattt tgtaggtaat tttaragtte	702
aactccaccc agetttcakt gaaggaacct ttcaaataat aratttttgc ttaccatara	762
raaaaratca aatgacaaag caaatattga ccattaagct ggaatatggt gataattgaa	822
cagttgtata aatgaaktaa ttgaattgta cacatacaat gggtgaattt tatggcatgt	882
caaagtatac ctcaataaag ctatttttt aaattgcmaa aaaaaaaaa	931

<210> 367

<211> 849

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 64..612

<221> sig_peptide

<222> 64..234

<223> Von Heijne matrix
 score 3.79999995231628
 seq QLWLVMEFCGAGS/VT

<221> polyA_site

<222> 839..849

<400> 367

acatacgggc aagttt	ataa gggtcgtcat	gtcaaaacgg	gccagcttgc as	gccatcaag 60
gtt atg gat gtc ac Met Asp Val Ti	ca ggg gat gaa nr Gly Asp Glu	gag gaa gaa Glu Glu Glu -50	atc aaa caa q Ile Lys Gln (	gaa att 108 Glu Ile
aac atg ttg aag a Asn Met Leu Lys Ly	aa tat tct cat ys Tyr Ser His -35	cac cgg aat	att gct aca	tac tat 156 Tyr Tyr
ggt gct ttt atc ac Gly Ala Phe Ile Ly	aa aag aac cca		gat gac caa	
ttg gtg atg gag tt Leu Val Met Glu Pl	t tgt ggt gct		acc gac ctg Thr Asp Leu	
aac aca aaa ggt aa Asn Thr Lys Gly A	ac acg ttg aaa	gag gag tgg Glu Glu Trp 15	att gca tac	atc tgc 300
msg gaa atc tta co	gg ggg ctg art rg Gly Leu Xaa 30	cac ctg cac	cag cat aaa	gtg att 348 Val Ile
cat cga rat att a His Arg Xaa Ile L	aa ggg caa aat ys Gly Gln Asn	gtc ttg ctg Val Leu Leu	act gaa aat	gca gaa 396 Ala Glu
40 gtt aaa cta gtg g. Val Lys Leu Val A	sp Phe Gly Xaa	akt gct cag Xaa Ala Gln 65	ctt gat cga	aca gtg 444 Thr Val 70
ggc agg arg aat a Gly Arg Xaa Asn T	hr Phe Ile Gly	act ccc tac	tgg atg gca Trp Met Ala	cca raa 492
gtt att gcc tgt g. Val Ile Ala Cys A	at gaa aac cca	sat gcc aca	tat gat ttc Tyr Asp Phe 100	aar art 540
gac ttg tgg tct t Asp Leu Trp Ser L	eu Gly Ile Thr	gcc att gaa	atg gca gaa	ggg ctc 588 Gly Leu
105 ccc ctc tct gtg a Pro Leu Ser Val T	ca tgc acc cca hr Cys Thr Pro	tgagagctct		ccggaatc 642
120	125		eesetestt s	ttgagaget 702
cagcgcctcg gctgaa	gtct aagaagtgg	t caaaaaatt	ccagicatit a	
gcttggtaaa aaatca	cage cagegacea	g caacagaaca	attgatgaag c	
tacgagacca acctaa		c gcattcaact	caaggaccat a	attgatagaa 822 849
caaagaagaa gcgagg	aaaa aaaaaaa			849

<210> 368

<211> 644

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 39..458

<221> sig_peptide

<222> 39..80 <223> Von Heijne matrix score 4.40000009536743 seq FLTALLWRGRIPG/RQ

<221> polyA_signal

<222> 613..618

<221> polyA site <222> 633..644 <400> 368 ageggagacy cagagtetty ageagegegn caggeace atg tto etg act geg etc 56 Met Phe Leu Thr Ala Leu etc tgg ege ege att ecc gge egt eaq tqq ate qqg aag eac eqq 104 Leu Trp Arg Gly Arg Ile Pro Gly Arg Gln Trp Ile Gly Lys His Arg - 5 cgg ccg cgg ttc gtg tcg ttg cgc gcc aag cag aac atg atc cgc cgc 152 Arg Pro Arg Phe Val Ser Leu Arg Ala Lys Gln Asn Met Ile Arg Arg 15 ctg gag atc gag gcg gag aac cat tac tgg ctg agc atg ccc tac atg 200 Leu Glu Ile Glu Ala Glu Asn His Tyr Trp Leu Ser Met Pro Tyr Met 30 35 acc cgg gag cag gag cgc ggc cac gcc gcg ttg cgc agg agg gag gcc 248 Thr Arg Glu Gln Glu Arg Gly His Ala Ala Leu Arg Arg Glu Ala tto gag god ata aag gog god god act too aag tto ood oog cat aga 296 Phe Glu Ala Ile Lys Ala Ala Ala Thr Ser Lys Phe Pro Pro His Arg 60 65 ttc att gcg gac cag ctc gac cat ctc aat vgt cac caa gaa atg gtc Phe Ile Ala Asp Gln Leu Asp His Leu Asn Xaa His Gln Glu Met Val 75 80 cta atc ctg agt cgt cac cct tgg att tta tgg atc acg gag ctg acc 392 Leu Ile Leu Ser Arg His Pro Trp Ile Leu Trp Ile Thr Glu Leu Thr 95 100 atc ttt acc tgg tct gga ctg aaa aac tgt agc ttg tgt gaa aat gag Ile Phe Thr Trp Ser Gly Leu Lys Asn Cys Ser Leu Cys Glu Asn Glu 110 115 488 ctt tgg acc agt ctt tat taaaacaaac aaacatgagt agtctgcata Leu Trp Thr Ser Leu Tyr 125 togaatatot agagototaa accoccoaat acttaaaagt otaattgotg tootgtggtt tcattagtct gataggaaga tagggatttc ctcagtcaca gatgatattt tgaaggaaag 608 644 ctgcaataaa gccacaatga tttgaaaaaa aaaaaa

<210> 369

<211> 918

<212> DNA

<213 > Homo sapiens

<220>

<221> CDS

<222> 9..185

<221> sig_peptide

<222> 9..50

<223> Von Heijne matrix
 score 3.70000004768372
 seq AALVTVLFTGVRR/LH

<221> polyA_site <222> 906..918

<400> 369

ageteage atg get get tta gtg act gtt etc tte aca ggt gte egg agg Met Ala Ala Leu Val Thr Val Leu Phe Thr Gly Val Arg Arg 50

ctg cac tgc agc gcr scg ctt ggg cgg gcc agt ggc grc tac agc	98
Leu His Cys Ser Ala Xaa Leu Gly Arg Ala Ala Ser Gly Xaa Tyr Ser	
1 10 15 agg aac tgg ctg cca acc cct ccg gct acg ggc ccc tta ccg agc tcc	146
Arg Asn Trp Leu Pro Thr Pro Pro Ala Thr Gly Pro Leu Pro Ser Ser	
20 25 30	
cag act ggt cat atg cgg atg gcc gcc ctg ctc ccc caa tgaaaggcca	195
Gln Thr Gly His Met Arg Met Ala Ala Leu Leu Pro Gln	
35 40 45	
gcttcgaaaa aaagctgaaa gggagacktt tgcaaracra kttgtactgc tgtcacagga	255
aatggacget ggattacaas catggcaset caggcagcar aakttgcagg aaraacaaag	315
gaagcaggaa aatgctctta aacccaaagg ggcttcactg aaaascccac ttccaaktca	375
ataaaaagca actcctgcct cccttcctca ccctgtctct ggatttcttt tctatcacct	435
aratgettea tecagecara aaatageett cackkteece atetgtette arageaaaar	495
agctgggacm ccaaraacaa gctgttarat cactgcctgg gaggcttggc ttartactct	555
catctctggt tocattccag ttcagctaag tcttgcttta aaatttttac ctcctagctg	615
ggtgcggtgg ctcacgcctg taatcccagc actttgggag gctgaggcgg gcagatcaca	675
agatcaggag ttcgagacca gcctggccaa cccagcctgg tcaacatggt gaaaccctgt	735
ccctactaaa gatacaaaca attagccggg cgtggtgggg tgcgcttgta atcccag:ta	795
ctcaggaggc tgaggcagga gaatcgctta aactcgggag gtagaggttg cagtgagcca	855 915
aggtcacacc attgcactcc aacctgggcg acagggcgag actctgtctc aaaaaaaaa	918
aaa	310
<210> 370	
<211> 472	
<212> DNA	
<213> Homo sapiens	
•	
<220>	
<221> CDS 45 45 45	
<222> 14316	
ik saab ach yo	
<221> sig_peptide - T'	
<222> 14121	
<223> Von Heijne matrix	
score 5.19999980926514	
seq PLRLLNLLILIEG/SV	
200 malya gignol	
<pre>&lt;221&gt; polyA_signal</pre>	
2222> 442447	
<221> polyA site	
<222> 458471	
<400> 370	
attatataga goc atg ggg cot tac aac gtg gca gtg cot toa gat gta	49
Met Gly Pro Tyr Asn Val Ala Val Pro Ser Asp Val	
-35 -30 -25	
tot cat god ogo tit tat tio tia tit cat oga oca tia agg otg tia	97
Ser His Ala Arg Phe Tyr Phe Leu Phe His Arg Pro Leu Arg Leu Leu	
-20 -15 -10	<b>.</b>
aat ctg ctc atc ctt att gag ggc agt gtc gtc ttc tat cag ctc tat	145
Asn Leu Leu Ile Leu Ile Glu Gly Ser Val Val Phe Tyr Gln Leu Tyr	
-5 1 5	
tee ttg etg egg teg gag aag tgg aac cac aca ett tee atg get ete	193
Ser Leu Leu Arg Ser Glu Lys Trp Asn His Thr Leu Ser Met Ala Leu	
10 15 20	241
ato oto tto tgo aac tac tat gtt tta ttt aaa ott oto ogg gac aga	241
Ile Leu Phe Cys Ash Tyr Tyr Val Leu Phe Lys Leu Leu Arg Asp Arg	
25 30 35 40	

WO 99/31236 -285- PCT/IB98/02122

wta kta								·				200
Xaa Xaa					Tyr !				Cyr (			289
aag gca Lys Ala		aa Ala		r Xaa		gaggga	igaa ci	caga	ataaa	3		336
aatattt attttgt. aaacaaa	tca tad	gttcta attatgt	t tttt t ttga	ttcttg	tga	ttttat agagtaa	aaata ggga	attta tatta	aa ga aa af	atatt	ttat	396 456 472
<210> 3° <211> 1° <212> D° <213> H°	504 NA	oiens										
<220>												
<221> C <222> 7		2										
	0234 on Hei core 4	jne mat .099999	904632									
		AALLASH	PIA/ EV	•								
<221> po	· -	_										
<221> p	olyA_s:	ite										
<222> 1	4931								٠			
_	71 gta gga ag atg Met	s04 acttccg cga aa Arg Ly	g gtg	gtt tt Val Le	r at u Il	t acc	ggg gc	t ag a Se	c ag	t gg	c att	60 111
<222> 1 <400> 3 agaaatc tgcgcga	71 gta gga ag atg Met -55	acttccg cga aa Arg Ly tc tgc	g gtg 's Val	gtt tt Val Le -9 g ctg	r at u Il so ctg	t acc of the following the thick the second	ggg gc Gly Al a gat	t ag a Se -4 gat	c ag r Se 5 gag	t gg r Gl ctt	c att y Ile cat	
<222> 1 <400> 3 agaaatc tgcgcga ggc ctg Gly Leu -40	71 gta gga ag atg Met -55 gcc c Ala L	acttccg cga aa Arg Ly tc tgc eu Cys	g gtg s Val aag cg Lys Ai	gtt tt Val Le -9 gg ctg rg Leu 35	r at u Il 50 ctg Leu	t acc e Thr gcg ga Ala Gl	ggg go Gly Al a gat u Asp -30	t ag a Se -4 gat Asp	c ag r Se 5 gag Glu	t gg r Gl ctt Leu	c att y Ile cat His	111
<222> 1 <400> 3 agaaatc tgcgcga  ggc ctg Gly Leu -40 ctg tgt Leu Cys -25	71 gta gg: ag atg Met -55 gcc c Ala L ttg g Leu A	acttccg cga aa Arg Ly tc tgc eu Cys cg tgc la Cys	g gtg s Val aag cg Lys Ai -: agg aa Arg As	gtt tt Val Le -5 gg ctg rg Leu 35 at atg sn Met	cr at u Il io ctg Leu agc Ser	e Thr gcg ga Ala Gl aag gc Lys Al	ggg gc Gly Al a gat u Asp -30 a gaa a Glu 5	t ag a Se -4 gat Asp gct Ala	c ag r Se 5 gag Glu gtc Val	t gg r Gl ctt Leu tgt Cys	c att y Ile cat His gct Ala -10	111
<222> 1 <400> 3 agaaatc tgcgcga  ggc ctg Gly Leu -40 ctg tgt Leu Cys	71 gta gg: ag atg Met -55 gcc c Ala L ttg g Leu A	acttccg cga aa Arg Ly tc tgc eu Cys cg tgc la Cys cc tct la Ser	g gtg s Val aag cg Lys Ai agg aa Arg As -20 cac co	gtt tt Val Le -5 gg ctg rg Leu 35 at atg sn Met	er at eu Il 50 ctg Leu agc Ser	e Thr gcg ga Ala Gl aag gc Lys Al	ggg gc Gly Al a gat u Asp -30 a gaa a Glu 5 c acc	t ag a Se -4 gat Asp gct Ala	c ager Session	t gg r Gl ctt Leu tgt Cys	c att y Ile cat His gct Ala -10 gtg	111
<222> 1 <400> 3 agaaatc tgcgcga  ggc ctg Gly Leu	71 gta gg; ag atg Met -55 gcc c Ala L ttg g Leu A ctg g Leu A	acttccg cga aa Arg Ly tc tgc eu Cys cg tgc la Cys cc tct la Ser -5 ac ctq	g gtg s Val aag cg Lys An -: agg aa Arg As -20 cac cc His P:	gtt tt Val Le -5 gg ctg rg Leu 35 at atg sn Met cc act ro Thr ca ttc er Phe	cr at the second of the second	e Thr gcg ga Ala Gl aag gc Lys Al -1 gag gt Glu Va 1 cgg gc	ggg gg Gly Al a gat u Asp -30 a gaa a Glu 5 c acc l Thr	a Se -4 gat Asp gct Ala att Ile aag Lys	c ager Se 5 gag Glu gtc Val gtc yal 5 gaa	ctt Leu tgt Cys cag Gln	c att y Ile cat His gct Ala -10 gtg Val aag	111 159 207
<222> 1 <400> 3 agaaatc tgcgcga  ggc ctg Gly Leu	71 gta ggg agg atgt -55 gcc Ala L ttg A ctg A ctg A ctg A	acttccg cga aa Arg Ly tc tgc eu Cys cg tgc la Cys cc tct la Ser -5 ac ctg sn Leu	g gtg s Val aag cg Lys An -: agg aa Arg As -20 cac cc His P: cag tc Gln S	gtt tt Val Le  19 19 19 10 10 10 10 10 10 10 10 10 10 10 10 10	er ateu Il 50 ctg Leu agc Ser gct Ala ttc Phe ata	e Thr gcg ga Ala Gl aag gc Lys Al -1 gag gt Glu Va 1 cgg gc Arg Al	a gat u Asp -30 a gaa a Glu c acc l Thr c tcc a Ser	a Se -4 gat Asp gct Ala att Ile aag Lys gct	c ager Se 5 gag Glu gtc Val 5 gaa Glu ggg	ctt Leu tgt Cys cag Gln ctt Leu	catt y Ile cat His gct Ala -10 gtg Val aag Lys atg	111 159 207 255
<222> 1 <400> 3 agaaatc tgcgcga  ggc ctg Gly Leu -40 ctg tgt Leu Cys -25 gct ctg Ala Leu gat gtc Asp Val caa agg Gln Arg	71 gta gg; ag atg -55 gcc c Ala L ttg g Leu A ctg g A ctg A	acttccg cga aa Arg Ly tc tgc eu Cys cg tgc la Cys cc tct la Ser -5 ac ctg sn Leu ag aga	ag gtg s Val aag cg Lys An agg aa Arg An -20 cac cc His P cag tc Gln S tta g Leu A	gtt tt Val Le  15 15 16 17 18 18 18 18 18 18 18 18 18 18 18 18 18	cr at the second of the second	e Thr gcg ga Ala Gl aag gc Lys Al -l gag gt Glu Va l cgg gc Arg Al tat ct Tyr Le	a gat u Asp -30 a gaa a Glu c acc l Thr c tcc a Ser a aat u Asn	a Se -4 gat Asp gct Ala att Ile aag Lys 20 gct Ala	c ager Se 5 gag Glu gtc Val 5 gaa Glu 999 Gly	ctt Leu tgt Cys cag Gln ctt Leu atc	catt y Ile cat His gct Ala -10 gtg Val aag Lys atg Met	111 159 207 255 303 351
<222> 1 <400> 3 agaaatc tgcgcga  ggc ctg Gly Leu -40 ctg tgt Leu Cys -25 gct ctg Ala Leu gat gtc Asp Val caa agg Gln Arg Cot aat	71 gta ggg ag atgt -55 gcc Ala L ttg A ctg A	acttccg cga aa Arg Ly tc tgc eu Cys cg tgc la Cys cc tct la Ser -5 ac ctg sn Leu ag aga iln Arg	ag gtg s Val aag cg Lys An agg aa Arg An -20 cac cc His P: cag tc Gln Sc tta g Leu A	gtt tt Val Le  19 ctg rg Leu 15 at atg sn Met 15 ac tr 15 ac tgt sp Cys 0 tc aaa	crateu Il io ctg Leu agc Ser gct Ala ttc Phe ata Ile	e Thr gcg ga Ala Gl aag gc Lys Al -l gag gt Glu Va l cgg gc Arg Al tat ct Tyr Le	a gat u Asp -30 a gaa a Glu c acc l Thr c tcc a Ser a aat u Asn l5 c ttt	t age -4 gat Asp gct atte agys 20ct a ggc	c age r Se 5 gag Glu gtc Val gtc Val 5 gaa Glu ggg Gly ctc	t gggr Gl ctt Leu tgt Cys cag Gln ctt Leu atc Ile	catt y Ile cat His gct Ala -10 gtg Val aag Lys atg Met tca	111 159 207 255 303
<222> 1 <400> 3 agaaatc tgcgcga  ggc ctg Gly Leu -40 ctg tgt Leu Cys -25 gct ctg Ala Leu gat gtc Asp Val caa agg Gln Arg cot aat Pro Asr 40	71 gta gg; ag atgt -55 gcc Ala L ttg g A Ctg A C	acttccg cga aa Arg Ly tc tgc eu Cys cg tgc la Cys cc tct la Ser -5 ac ctg sn Leu ag aga iln Arg	agg gtg S Val  aag cg Lys An  -: agg aa Arg As  -20 cac cc His P: cag tc Gln S  tta g Leu A  , 3 aat a Asn I	gtt tt Val Le  -5 gg ctg rg Leu 35 at atg sn Met cc act ro Thr ca ttc er Phe 15 ac tgt sp Cys 0 tc aaa le Lys	agc Ser gct Ala ttc Phe ata Ile gca Ala	e Thr gcg ga Ala Gl aag gc Lys Al gag gt Glu Va l cgg gc Arg Al tat ct Tyr Le ctt tt Leu Ph	a gat u Asp -30 a gaa a Glu 5 c acc l Thr c a Ser a aat u Asn 35 c ttt	et age a Se -4 gat Asp gct Ala att Ile aag Lys 20 gct Ala ggcy Ala	c aggr Se 5 gag Glu gtc Val 5 gaa Glu ggg Gly ctc Leu	t gggr Gl ctt Leu tgt Cys cag Gln ctt Leu atc Ile ttt Phe	c att y Ile cat His gct Ala -10 gtg Val aag Lys atg Met tca Ser 55	111 159 207 255 303 351
<222> 1 <400> 3 agaaatc tgcgcga  ggc ctg Gly Leu -40 ctg tgt Leu Cys -25 gct ctg Ala Leu gat gtc Asp Val caa agg Gln Arg 25 cct aat Pro Asr	71 gta ggg ag atgt -55 gcc Ala L ttg A ctg A	acttccg cga aa Arg Ly tc tgc eu Cys cg tgc la Cys cc tct la Ser -5 ac ctg sn Leu ag aga iln Arg	agg gtg gtg s Val  aag cg Lys An  agg aa  Arg As  -20  cac cc His P:  cag tc Gln Sc  tta gg Leu A  ,	gtt tt Val Le  29 ctg rg Leu 35 at atg sn Met cc act ro Thr ca ttc er Phe 15 ac tgt sp Cys 0 tc aaa le Lys tc tcc	agc Ser gct Ala ttc Phe ata Ile gca Ala aca	e Thr  gcg ga Ala Gl  aag gc Lys Al  gag gt Glu Va 1 cgg gc Arg Al  tat ct Tyr Le  ctt tt Leu Ph	a gat a gat a gat a gat a gaa a Glu cac a cac a a a a a a a a a a a a a a	t age -4 gat Asp gct Ala att Ile agg Lys gct Ala ggy Ctg	c age r Se 5 gag Glu gtc Val gtc Val 5 gaa Glu ggg Gly ctc Leu ctg	t gggr Gl ctt Leu tgt Cys cag Gln ctt Leu atc Ile tttt Phe	c att y Ile cat His gct Ala -10 gtg Val aag Lys atg Met tca Ser 55 cag	111 159 207 255 303 351 399

								cgg Arg								543
	_	gac				_	ctc	atc Ile				tct	_	_	_	591
								gac Asp								639
			_					gcc Ala		_		_	-			687
ttg Leu	aac Asn	agg Arg	aac Asn 155	ttc Phe	aac Asn	cag Gln	cag Gln	ggt Gly 160	ctc Leu	tat Tyr	ccc Ser	aat Asn	gtg Val 165	gcc Ala	tgt Cys	735
	_			_				aca Thr								783
								ata Ile								831
								aat Asn								879
ctt	ttc Phe	cac His	caa Gln	aag Lys 220	cct Pro	gaa Glu	tct Ser	ctc Leu	aat Asn 225	cct Pro	ctg Leu	atc Ile	aaa Lys	tat Tyr 230	ctg Leu	927
agt Ser	gcc Ala	acc Thr	act Thr 235	ggc	ttt Phe	gga Gly	aga Arg	aat Asn 240	Tyr	att Ile	atg Met	acc Thr	cag Gln 245	aag Lys	atg Met	975
gac Asp	cta Leu	gat Asp 250	gaa Glu	gac Asp	act Thr	gct Ala	gaa Glu 255	aaa Lys	Phe	Tyr	Gln	aag Lys 260	tta Leu	ctg Leu	gaa Glu	1023
ctg Leu	gaa Glu 265	aag Lys	cac His	att Ile	agg Arg	gtc Val 270	act Thr	att Ile	caa Gln	aaa Lys	aca Thr 275	gat Asp	aat Asn	cag Gln	gcc Ala	1071
	ctc Leu						taa	ttcc	agc a	actt	tggg	ag g	ccaa	ggca	g	1122
aag	gatca	act t	tgaga	acca	gg ag	gttc	aaga	c ca	gcct	gaga	aac	atag	tga	gccc	ttgtct	1182
ctad	caaaa	aag a	aaata	aaaa	at a	atag	ctgg	g tg	tggt	ggca	tgc	gcat	gta	gtcc	cagcta	1242
ctca	agaaq	gga 1	tgag	gtgg	ga g	gate	tctt	g ag	gctg	ggag	gca	gagg	ttg	cagt	gagetg	1302 1362
agai	tgt	gcc a	actg	cact	cc aq	gcct	gggc	g ac	agcg	agac	cct	gtct	caa	aata	tgtata	1422
tati	caal	lat i	acaca	acaa:	aa C	artt	ctac	t ca	atro	gata	ata	taca	ttt	gtaa	accttc taaact	1482
	aacta							2 34	J- <b>-3</b>	J4				J		1504

```
<210> 372
```

<211> 765

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 274..597

<221> sig_peptide <222> 274..399 <223> Von Heijne matrix score 5.19999980926514

### seg LLFDLVCHEFCQS/DD

<221> polyA_signal <222> 731..736 <221> polyA site <222> 754..765 <400> 372 accaggaaca tocagctatt tatgatagca tttgcttcat tatgtcaagt tcaacaaatg 60 ttgacttgct ggtgaaggtg ggggaggttg tggacaagct ctttgatttg gatgagaaac 120 taatgttaag aatgggtcag aaatggggct gctcagcctc tggaccaacc ccaggaagag 180 totgaagago agocagtgtt toggottgtg cootgtatac ttgaagotgo caaacaagta 240 cgttctgaaa atccagaatg gcttgatgtt tac atg cac att tta caa ctg ctt 294 Met His Ile Leu Gln Leu Leu -40 act aca gtg gat gat gga att caa gca att gta cat tgt cct gac act 342 Thr Thr Val Asp Asp Gly Ile Gln Ala Ile Val His Cys Pro Asp Thr -30 -25 gga aaa gac att tgg aat tta ctt ttt gac ctg gtc tgc cat gaa ttc 390 Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp Leu Val Cys His Glu Phe - 15 -10 tgc cag tct gat gat cca gcc atc att ctt caa raa car aaa acr gtg Cys Gln Ser Asp Asp Pro Ala Ile Ile Leu Gln Xaa Gln Lys Thr Val 1 5 cta gcc tct gtt ttt tca gtg ttg tct gcc atc tat gcc tca cag act 486 Leu Ala Ser Val Phe Ser Val Leu Ser Ala Ile Tyr Ala Ser Gln Thr 20 25 gag caa gak tat cta aar ata raa aaa gga gac ggt ggc tca ggg agt Glu Gln Xaa Tyr Leu Lys Ile Xaa Lys Gly Asp Gly Gly Ser Gly Ser 35 40 582 aaa gga agg cca ktt gan caa aca gaa ktg ttc ctc tgc att tca aaa Lys Gly Arg Pro Xaa Xaa Gln Thr Glu Xaa Phe Leu Cys Ile Ser Lys 50 55 . cct tct tcc ttt cta tagccctgtg gtggaagatt ttattaaaat cctacgtgaa 637 Pro Ser Ser Phe Leu 697 gttgataagg cgcttgctga tgacttggaa aaaaacttcc caagtttgaa ggttcagact 757 taaaacctga attggaatta cttctgtaca agaaataaac tttatttttc tcactgacaa

765

<210> 373 <211> 1041 <212> DNA

aaaaaaa

<213> Homo sapiens

<220>

<221> CDS

<222> 230..469

<221> sig_peptide

<222> 230..307

<223> Von Heijne matrix score 4.90000009536743 seq VLCTNOVLITARA/VP

<221> polyA_signal <222> 1004..1009

<221> polyA_site

<222> 1027..1040

<400> 373	
aacttccaag ttgtagtgtt gttgttttca gcctgctgct gctgctgcta ttgcggctag	60
gggaaccgtc gtggggaagg atggtgtgcg aaaaatgtga aaagaaactt ggtactgtta	120
tcactccaga tacatggaaa gatggtgcta ggaataccac agaaagtggt ggaagaaagc	180
tgaatgaaaa taaagctttg acttcaaaaa aagccagaat tgatccata atg gaa gaa	238
Met Glu Glu	
-25	
ata agt tot coa off gta gaa tit gta aaa gtt tig tgc acc aac cag	286
Ile Ser Ser Pro Leu Val Glu Phe Val Lys Val Leu Cys Thr Asn Gln	
-20 -15 -10	
gtt ctc att act gcc agg gct gtg cct aca aaa aag gca tct gtg cga	334
Val Leu Ile Thr Ala Arg Ala Val Pro Thr Lys Lys Ala Ser Val Arg	
-5 1 5	
tgt gtg gaa aaa agg ttt tgg ata cca aaa act aca agc aaa cat ctg	382
Cys Val Glu Lys Arg Phe Trp Ile Pro Lys Thr Thr Ser Lys His Leu	
10 15 20 25	
tet aga tgt att gat gga att tet gge ttt eta aat gat ttt aet tte	430
Ser Arg Cys Ile Asp Gly Ile Ser Gly Phe Leu Asn Asp Phe Thr Phe	
30 35 40	470
tgc ctt gaa ttt tca agg cat aga tgt caa ctt aca gaa taacatgtkt	479
Cys Leu Glu Phe Ser Arg His Arg Cys Gln Leu Thr Glu	
45 50	539
taagataatt aagtktaaac cagaraattt gattgttact cattttgctc tcatgtkcta	599
aaacagcaac agtgtaacta gtcttttgtt gtaaatggtt attttcctta taaaaatttt	659
aaaaactaag tggcaaatte catgaaaata ttteteagtt etgtatgcac ttttatttaa	719
cattattcat ataattctcc ccccaccact ttatttat	779
agataataaa tactttgctc tgaatttggc atccaaagtt aacatttctc ccctcactcc	839
cttgctggtg tcatagttat tagaatcagc agcctcttaa ctaattgcgg tttcatagga	899
tatataaatg tttcaagcca ttattgctga atggttcttt agttattaac ctagacccaa atcaaagacc agttggattt atgatatttt ttatttgttc ttgcagccaa agtgccagtt	959
tetttaatat gtgaccaaga acacaaggag catecatatg gecaaataaa tacaetgaat	1019
	1041
tttagaaaaa caaaaaaaaa ar	

<210> 374 <211> 1164 <212> DNA <213> Homo sapiens <220> <221> CDS

<221> sig_peptide <222> 72..203

<222> 72..545

<223> Von Heijne matrix score 5.5 seq ILFFTGWWIMIDA/AV

<221> polyA_site <222> 1151..1162

	-30					-25					-20					
gca	ggt	ata	ttg	ttt	ttt	aca	ggc	tgg	tgg	ata	atg	att	gat	gca	gct	206
	Gly	Ile	Leu	Phe		Thr	Gly	Trp	Trp		Met	Ile	Asp	Ala		
-15					-10					-5					1	
	gtg			_		-	•	_			_				_	254
vai	Val	Tyr	Pro	Lys	PIO	GIU	Gin	10	Asn	HIS	Ala	Pne	15	Inr	Cys	
aat	gta	+++	tcc	aca	tta	act	ttc		ato	ага	aat	act		tee	aat	302
	Val				_	-			•			_	-			***
•		20					25					30				
gct	cag	gtg	aga	ggt	gat	agc	tat	ġaa	agc	ggc	tgt	tta	gga	aga	aca	350
Ala	Gln	Val	Arg	Gly	Asp	Ser	Tyr	Glu	Ser	Gly	Cys	Leu	Gly	Arg	Thr	
	35					40					45					
	gct	_	_							-	_	_				398
51y	Ala	Arg	Val	rrp	55	Pne	116	GIY	Pne	me C	ren	met	Pne	GIY	5E1 65	
	att	act	tcc	atq		att	ctt	ttt	aat		tat	att	acc	caa		446
	Ile	_		-						-		-				
				70	•				75		•			80		
act	gat	gtt	tat	ccg	gga	cta	gct	gtg	ttt	ttt	çaa	aat	gca	ctt	ata	494
Thr	Asp	Val	•	Pro	Gly	Leu	Ala		Phe	Phe	Gln	Asn		Leu	Ile	
			85					90					95			- 40
	ttt	-		_						_		-				542
Pne	Phe	100	inr	Leu	IIe	lyr	105	Pne	GIY	Arg	inr	110	GIU	reu	IIp	
acc	tgag		act t	ctta	agto	a ca		tecti	t tto	tta	tatt		ttta	tag		595
Thr	- 5 ,	,								,		5				
ata	ggttt	ctt t	atct	ctca	ag ta	acaca	attg	caa	aatg	gagt	aga	ttgt	aca	ttaa	atgttt	655
															tatttt	
															tgagta	775
	_				_	_		_			_				catcat	835 895
	-		_	_			-								tgcctg	955
															tgagac gcatgg	1015
_					-										gaaccc	1075
															gagaaa	1135
	aaact				-	-	_	-	_			_				1164

```
<210> 375
```

<220>

<221> CDS

<222> 36..425

<221> sig_peptide <222> 36..119

<223> Von Heijne matrix score 11.6000003814697 seq LLLLVQLLRFLRA/DG

<221> polyA_signal <222> 1215..1220

<221> polyA_site

<222> 1240..1250

<400> 375

<211> 1250

<212> DNA

<213> Homo sapiens

atttetteee eeegagetgg gegtgegegg eegea atg aac tgg gag etg etg Met Asn Trp Glu Leu Leu -25	53
ctg tgg ctg Ctg gtg ctg tgc gcg Ctg Ctc ctg ctc ttg gtg cag ctg Leu Trp Leu Leu Val Leu Cys Ala Leu Leu Leu Leu Val Gln Leu -20 -15 -10	101
ctg cgc ttc ctg agg gct gac ggc gac ctg acg cta cta tgg gcc gag Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu Leu Trp Ala Glu -5 10	149
tgg cag gga cga cgc cca gaa tgg gag ctg act gat atg gtg gtg tgg Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp Met Val Val Trp 15 20 25	197
gtg act gga gcc tcg agt gga att ggt gag gag ctg gct tac cag ttg Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu Ala Tyr Gln Leu 30 35 40	245
tct aaa cta gga gtt tct ctt gtg ctg tca gcc aga aga gtg cat gag Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg Arg Val His Glu 45 50 55	-293
ctg gaa agg gtg aaa aga aga tgc cta gag aat ggc aat tta aaa gaa Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly Asn Leu Lys Glu 60 65 70	341
aaa gat ata ctt gtt ttg ccc ctt gac ctg acc gac act ggt tcc cat Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp Thr Gly Ser His 75 80 85 90	389
gaa agc ggc tac caa agc tgt tct cca gga att tgg tagaatcgac Glu Ser Gly Tyr Gln Ser Cys Ser Pro Gly Ile Trp 95	435
attotggtca acaatgtgga aatgtcccag cgttctctgt gcatggatac caacttggat	495
gtotacagaa agotaatgag agottaacta ottagggacg gtgtcottga caaaatgtgk	555
kctgcctcac atgatcgaga ngaarcaagg aaagattgtt actgtgaata gcatcctggg	615
tatcatatot gtacotottt coattggata otgtgotago aagoatgoto tooggggktk	675
ktttaatggc cttcraacag aacttgccac atacccargt ataatagttt ctaacatttg	735
cccaggacct gtgcaatcaa atattgtgga aaattcccta gctggagaag tcacaaagac	795
tataggcaat aatggagacc agtcccacaa gatgacaacc agtcgttgtg tgcggctgat	855 915
gttaatcagc atggccaatg atttgaaaga agtttggatc tcagaacaac ctttcttgtt	975
agtaacatat ttgtggcaat acatgccaac ctgggcctgg tggataacca acaagatggg gaagaaaagg attgagaact ttaagagtgg tgtggatgca gactcttctt attttaaaat	1035
ctttaagaca aaacatgact gaaaagagca cctgtacttt tcaagccact ggagggagaa	1095
atggaaaaca tgaaaacagc aatcttctta tgcttctgaa taatcaaaga ctaatttgtg	1155
attttacttt ttaatagata tgactttgct tccaacatgg aatgaaataa aaaataaata	1215
ataaaagatt gccatgaatc ttgcaaaaaa aaaaa	1250

```
<210> .376
```

<211> 947

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 155..751

<221> sig_peptide <222> 155..340

<223> Von Heijne matrix score 3.70000004768372 seq SILGIISVPLSIG/YC

<221> polyA_signal <222> 912..917

<221> polyA site

<222> 937..947 <400> 376 agtgaaaaga agatgcctag agaatggcaa tttaaaagaa aaagatatac ttgttttgcc cettgacetg accgacactg gttcccatga ageggetace aaagetgtte tecaggagtt tggtagaate gacattetgg teaacaatgg tgga atg tee cag egt tet etg tge Met Ser Gln Arg Ser Leu Cys -60 atg gat acc agc ttg gat gtc tac aga rag cta ata gag ctt aac tac Met Asp Thr Ser Leu Asp Val Tyr Arg Xaa Leu Ile Glu Leu Asn Tyr 223 -50 -45 tta ggg acg gtg tcc ttg aca aaa tgt gtt ctg cct cac atg atc gag Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His Met Ile Glu 271 - 35 -30 agg aag caa gga aag att gtt act gtg aat agc atc ctg ggt atc ata Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu Gly Ile Ile -20 ~10 tot gta cot ott too att gga tao tgt got ago aag cat got oto ogg Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His Ala Leu Arg 367 ggt ttt ttt aat ggc ctt cga aca gaa ctt gcc aca tac cca ggt ata Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly Ile 415 15 20 ata gtt tct aac att tgc cca gga cct gtg caa tca aat att gtg gaa Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn Ile Val Glu 463 30 35 aat too ota got gga gaa gto aca aaa act ata ggo aat aat gga aac Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn Asn Gly Asn 511 50 cag tee cae aag atg aca ace agt egt tgt gtg egg etg atg tta ate Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu Ile 559 age atg gcc aat gat ttg aaa gaa gtt tgg ate tca gaa caa cet tte Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Gln Pro Phe 607 80 ttg tta gta aca tat ttg tgg caa tac atg cca acc tgg gcc tgg tgg 655 Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp Ala Trp Trp 95 100 ata acc aac aag atg ggg aag aaa agg att gag aac ttt aag agt ggt 703 Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe Lys Ser Gly 110 115 gtg gat gcm rac tet tet tat ttt aaa ate ttt aag aca aaa cat gae 751 Val Asp Ala Xaa Ser Ser Tyr Phe Lys Ile Phe Lys Thr Lys His Asp 125 130 tgaaaaganc acctgtactt ttcaagccac tggagggaga aatggaaaac atgaaaacag caatcttctt atgcttctga ataatcaaag actaatttgt gattttactt tttaatagat 811 871 atgactttgc ttccaacatg grrtgaaata aaaaataaat aataaaagat tgccatgrrt 931 cttgcaaaaa aaaaaa

```
<210> 377
<211> 621
<212> DNA
```

<220> <221> CDS <222> 46..585

<221> sig peptide

<213> Homo sapiens

<222> 46..120 <223> Von Heijne matrix score 6.30000019073486 seg AFSLSVMAALTFG/CF <221> polyA_signal <222> 584..589 <221> polyA_site <222> 606..619 <400> 377 aactgggtgt gcgtrtggag tccggactcg tgggagacga tcgcg atg aac acg gtg Met Asn Thr Val 105 ctg tcg cgg gcg aac tca ctg ttc gcc ttc tcg ctg agc gtg atg gcs Leu Ser Arg Ala Asn Ser Leu Phe Ala Phe Ser Leu Ser Val Met Ala -15 -10 geg etc acc ttc ggc tgc ttc atc ayy acc gcc ttc aaa gac agg agc 153 Ala Leu Thr Phe Gly Cys Phe Ile Xaa Thr Ala Phe Lys Asp Arg Ser 5 gtc ccg gtg cgg ctg cac gtc tcg cga atc atg cta aaa aat gta gaa 201 Val Pro Val Arg Leu His Val Ser Arg Ile Met Leu Lys Asn Val Glu 20 gat ttc act gga cct aga gaa aga agt gat ctg gga ttt atc aca ttt Asp Phe Thr Gly Pro Arg Glu Arg Ser Asp Leu Gly Phe Ile Thr Phe 35 297 gat ata act gct gat cta gag aat ata ttt gat tgg aat gtt aag cag Asp Ile Thr Ala Asp Leu Glu Asn Ile Phe Asp Trp Asn Val Lys Gln 55 50 ttg ttt ctt tat tta tca gca gaa tat tca aca aaa aat aat gct ctg 345 Leu Phe Leu Tyr Leu Ser Ala Glu Tyr Ser Thr Lys Asn Asn Ala Leu 70 65 393 aac caa ktt gtc cta tgg gac aag att gtt ttg aga ggt gat aat ccg Asn Gln Xaa Val Leu Trp Asp Lys Ile Val Leu Arg Gly Asp Asn Pro 85 80 aag ctg ctg ctg aaa gat atg aaa aca aaa tat ttt ttc ttt gac gat 441 Lys Leu Leu Lys Asp Met Lys Thr Lys Tyr Phe Phe Asp Asp 100 105 489 gga aat ggt ctc wag gga aac agg aat gtc act ttg acc ctg tct tgg

Gly Asn Gly Leu Xaa Gly Asn Arg Asn Val Thr Leu Thr Leu Ser Trp

Asn Val Val Pro Asn Ala Gly Ile Leu Pro Leu Val Thr Gly Ser Gly

cac gta tot gto coa ttt coa gat aca tat gaa ata acg aag agt tat His Val Ser Val Pro Phe Pro Asp Thr Tyr Glu Ile Thr Lys Ser Tyr

115 aac gtc gta cca aat gct gga att cta cct ctt gtg aca gga tca gga

130

145

taaattatto tgaatttgaa acaaaaaaa aaaahm

120

150

537

585

621

<210> 378

<211> 52

<212> PRT

<213> Homo sapiens

110

<220>

<221> SIGNAL

<222> -20..-1

<400> 378

<210> 379 <211> 193 <212> PRT <213> Homo sapiens . <220> <221> SIGNAL <222> -23..-1 <400> 379 Met Val Val Leu Arg Ala Gly Lys Lys Thr Phe Leu Pro Pro Leu Xaa -15 -10 -20 Arg Ala Phe Ala Cys Arg Gly Cys Gln Leu Ala Pro Glu Arg Gly Ala Glu Arg Arg Asp Thr Ala Pro Ser Gly Val Ser Arg Phe Cys Pro Pro 15 20 Arg Lys Ser Cys His Asp Trp Ile Gly Pro Pro Asp Lys Tyr Ser Asn 30 35 Leu Arg Pro Val His Phe Tyr Ile Pro Glu Asn Glu Ser Pro Leu Glu 50 Gln Lys Leu Arg Lys Leu Arg Gln Glu Thr Gln Glu Trp Asn Gln Gln 65 Phe Trp Ala Asn Gln Asn Leu Thr Phe Ser Lys Glu Lys Glu Glu Phe 80 85 Ile His Ser Arg Leu Lys Thr Lys Gly Leu Gly Leu Arg Thr Glu Ser 95 100 Gly Gln Lys Ala Thr Leu Asn Ala Glu Glu Met Ala Asp Phe Tyr Lys 110 115 120 Glu Phe Leu Ser Lys Asn Phe Gln Lys His Met Tyr Tyr Asn Arg Asp 125 130 Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly Lys Val Ala 145 150 Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys Lys Arg Ser 160 Asn 170

<210> 380 <211> 82 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -14. -1

Met Ala Phe Thr Leu Xaa Ser Leu Leu Gln Ala Ala Leu Leu Cys Val

WO 99/31236 -294 - PCT/IB98/02122

<210> 381 <211> 198 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -21..-1

<400> 381 Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala Leu Ala Met Val Thr -15 Arg Pro Ala Ser Ala Ala Pro Met Gly Gly Pro Glu Leu Ala Gln His Glu Glu Leu Thr Leu Leu Phe His Gly Thr Leu Gln Leu Gly Gln Ala 20 15 Leu Asn Gly Val Tyr Arg Thr Thr Glu Gly Arg Leu Thr Lys Ala Arg 35 30 Asn Ser Leu Gly Leu Tyr Gly Arg Thr Ile Glu Leu Leu Gly Gln Glu 50 Val Ser Arg Gly Arg Asp Ala Ala Gln Glu Leu Arg Ala Ser Leu Leu 65 70 Glu Thr Gln Met Glu Glu Asp Ile Leu Xaa Leu Gln Ala Xaa Ala Thr 85 80 Ala Glu Val Leu Gly Glu Val Ala Gln Ala Gln Lys Val Leu Arg Asp 100 105 Ser Val Gln Arg Leu Xaa Xaa Gln Leu Xaa Xaa Ala Trp Leu Gly Pro 120 115 110 Ala Tyr Arg Lys Phe Glu Val Leu Lys Ala Pro Pro Xaa Lys Gln Asn 135 130 125 His Ile Leu Trp Ala Leu Thr Gly His Val Xaa Arg Gln Xaa Arg Glu 145 150 Met Val Ala Gln Gln Xaa Xaa Leu Xaa Gln Ile Gln Glu Lys Leu His 160 165

<210> 382 <211> 160 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -55..-1

Thr Ala Ala Leu Pro Ala 175

<400> 382 Met Asp Lys Leu Lys Lys Val Leu Ser Gly Gln Asp Thr Glu Asp Arg

-50 -45 Ser Gly Leu Ser Glu Val Val Glu Ala Ser Ser Leu Ser Trp Ser Thr -30 -25 - 35 Arg Ile Lys Gly Phe Ile Ala Cys Phe Ala Ile Gly Ile Leu Cys Ser -15 -10 Leu Leu Gly Thr Val Leu Leu Trp Val Pro Arg Lys Gly Leu His Leu - 5 5 1 Phe Ala Val Phe Tyr Thr Phe Gly Asn Ile Ala Ser Ile Gly Ser Thr 15 20 Ile Phe Leu Met Gly Pro Val Lys Gln Leu Lys Arg Met Phe Glu Pro Thr Arg Leu Ile Ala Thr Ile Met Val Leu Leu Cys Phe Ala Leu Thr 50 Leu Cys Ser Ala Phe Trp Trp His Asn Lys Gly Leu Ala Leu Ile Phe 65 Cys Ile Leu Gln Ser Leu Ala Let Thr Trp Tyr Ser Leu Ser Phe Ile 80 85 Pro Phe Ala Arg Asp Ala Val Lys Xaa Cys Phe Ala Val Cys Leu Ala 90 . 95

<210> 383 <211> 108 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -18..-1

<210> 384 <211> 64 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -22..-1

<400> 384
Met Ile Ser Arg Gln Leu Arg Ser Leu Ser Cys Leu Cys Pro Ala Leu
-20 -15 -10
Phe Pro GIy Thr Ser Ser Phe Ile Val Ala Leu Ser Ser Pro Ala Asp

WO 99/31236 -296- PCT/IB98/02122

```
Leu Tyr Ile Pro Xaa Arg Xaa Arg Ser Asp Glu Leu Val Phe Glu Ser
           15
                        20
Gln Lys Gly Ser Ala Met Glu Leu Ala Val Ile Thr Val Xaa Gly Val
                         35
<210> 385
<211> 27
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
Met Gly Phe Leu Xaa Leu Met Thr Leu Thr Thr His Val His Ser Ser
-15 -10
Ala Lys Pro Asn Glu Gln Pro Trp Leu Leu Asn
          5
                           10
<210> 386
<211> 186
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 386
Met Ser Pro Ser Gly Arg Leu Cys Leu Leu Thr Ile Val Gly Leu Ile
 -20 -15
                           -10
Leu Pro Thr Arg Gly Gln Thr Leu Lys Asp Thr Thr Ser Ser Ser Ser
                               5
                  1
Ala Asp Ser Thr Ile Met Asp Ile Gln Val Pro Thr Arg Ala Pro Asp
                                             25
                            20
        15
Ala Val Tyr Thr Glu Leu Gln Pro Thr Ser Pro Thr Pro Thr Trp Pro
                       35
                                          40
    30
Ala Asp Glu Thr Pro Gln Pro Gln Thr Gln Thr Gln Gln Leu Glu Gly
                     50
                                       55
Thr Asp Gly Pro Leu Val Thr Asp Pro Glu Thr His Xaa Ser Xaa Lys
                                    70
                 65
Ala Ala His Pro Thr Asp Asp Thr Thr Thr Leu Ser Glu Arg Pro Ser
                                 85
              80
Pro Ser Thr Xaa Val His Xaa Arg Pro Xaa Xaa Pro Ser Xaa His Leu
                                            105
                             100
Val Phe Met Arg Met Thr Pro Ser Ser Met Met Asn Thr Pro Ser Gly
                                 120
       110
                         115
Asn Xaa Gly Cys Trp Ser Gln Leu Cys Cys Ser Ser Gln Ala Ser Ser
                                       135
                     130
Ser Ser Pro Val Ala Ser Ala Gly Ser Cys Pro Gly Tyr Ala Gly Ile
               145
Ile Ala Gly Glu Ser Ile Arg Asn Arg Ser
              160
```

```
<210> 387
<211> 179
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
<400> 387
Met Glu Thr Gly Ala Leu Arg Arg Pro Gln Leu Leu Pro Leu Leu
                        -20
                                          -15
Leu Leu Cys Gly Pro Ser Gln Asp Gln Cys Arg Pro Val Leu Gln Asn
                   - 5
Leu Leu Gln Ser Pro Gly Leu Thr Trp Ser Leu Glu Val Pro Thr Gly
                              15
          10
Arg Glu Gly Lys Glu Gly Gly Asp Arg Gly Pro Gly Leu Xaa Gly Ala
                          30
Thr Pro Ala Arg Ser Pro Gln Gly Lys Glu Met Gly Arg Gln Arg Th
                                         50
                    4.5
Arg Lys Val Lys Gly Pro Ala Trp Xaa His Thr Ala Asn Gln Glu Leu
                                      65
                   60
Asn Arg Met Arg Ser Leu Ser Ser Gly Ser Val Pro Val Gly His Leu
                                  80
               75
Glu Gly Gly Thr Val Lys Leu Gln Lys Asp Thr Gly Leu His Ser Cys
                              95
Xaa Asp Gly Met Ala Ser Leu Glu Gly Thr Pro Ala Ser Val Leu Ala
                          110
                                             115
Asp Ala Cys Pro Gly Phe His Asp Val Xaa Val Gln Xaa Ala Leu Phe
                    125
                                          130
Gly Leu Ser Gly Xaa Xaa Leu Trp Leu Lys Thr His Phe Cys Leu Ser
                140
                                      145
Ile Xaa Leu
<210> 388
<211> 150
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -55..-1
Met Ala Thr Thr Val Pro Asp Gly Cys Arg Asn Gly Leu Lys Ser Lys
                                       -45
-55
                    -50
Tyr Tyr Arg Leu Cys Asp Lys Ala Glu Ala Trp Gly Ile Val Leu Glu
                                   -30
                -35
Thr Val Ala Thr Ala Gly Val Val Thr Ser Val Ala Phe Met Leu Thr
                                -15
                                                  -10
            -20
Leu Pro Ile Leu Val Cys Lys Val Gln Asp Ser Asn Arg Arg Lys Met
Leu Pro Thr Gln Phe Leu Phe Leu Leu Gly Val Leu Gly Ile Phe Gly
```

20

35

Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp Gly Ser Thr Gly Pro Thr

Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser Ile Cys Phe Ser Cys Leu 50

Leu Ala His Ala Val Ser Leu Thr Lys Leu Val Arg Gly Arg Lys Ala

65

15

30

45

pro Phe Pro Val Gly Asp Ser Gly Ser Gly Arg Gly Leu Gln Pro Ser

Pro Gly Cys Tyr Arg Tyr

```
90
<210> 389
<211> 236
<212> PRT
<213 > Homo sapiens
<220>
<221> SIGNAL
<222> -31..-1
<400> 389
Met Leu Ser Lys Gly Leu Lys Arg Lys Arg Glu Glu Glu Glu Lys
                     -25
Glu Pro Leu Ala Val Asp Ser Trp Trp Leu Asp Pro Gly His Ala Ala
-15
                   -10
                                   -5
Val Ala Gln Ala Pro Pro Ala Val Ala Ser Ser Ser Leu Phe Asp Leu
                             10
Ser Val Leu Lys Leu His His Ser Leu Gln Xaa Ser Xaa Pro Asp Leu
                           25
                                              30
      20
Arg His Leu Val Leu Val Xaa Asn Thr Leu Arg Arg Ile Gln Ala Ser
                       40
                                           45
Met Ala Pro Ala Ala Ala Leu Pro Pro Val Pro Thr Pro Pro Ala Ala
                                       60
                   55
Pro Xaa Val Ala Asp Asn Leu Leu Ala Ser Ser Asp Ala Ala Leu Ser
                                   75
Ala Ser Met Ala Xaa Leu Leu Glu Asp Leu Ser His Ile Glu Gly Leu
                              90
Ser Gln Ala Pro Gln Pro Leu Ala Asp Glu Gly Pro Pro Gly Arg Ser
       100
                                              110
                          105
Ile Gly Gly Xaa Pro Pro Xaa Leu Gly Ala Leu Asp Leu Leu Gly Pro
                                          125
   115
                      120
Ala Thr Gly Cys Leu Leu Asp Asn Gly Leu Glu Gly Leu Phe Glu Asp
                                      140
                  135
Ile Asp Thr Ser Met Tyr Asp Asn Glu Leu Trp Ala Pro Ala Ser Glu
                                   155
               150
Gly Leu Lys Pro Gly Pro Glu Asp Gly Pro Gly Lys Glu Glu Ala Pro
                                                  175
                               170
          165
Glu Leu Asp Glu Ala Glu Leu Asp Tyr Leu Met Asp Val Leu Val Gly
                           185
Thr Gln Ala Leu Glu Arg Pro Pro Gly Pro Gly Arg
                        200
<210> 390
<211> 149
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -100..-1
<400> 390
Met Glu Thr Leu Tyr Arg Val Pro Phe Leu Val Leu Glu Cys Pro Asn
                                       - 90
```

- 95

Leu Lys Leu Lys Lys Pro Pro Trp Leu His Met Prc Ser Ala Met Thr -80 -75 Val Tyr Ala Leu Val Val Val Ser Tyr Phe Leu Ile Thr Gly Gly Ile -55 -65 -60 Ile Tyr Asp Val Ile Val Glu Pro Pro Ser Val Gly Ser Met Thr Asp -45 -40 Glu His Gly His Gln Arg Pro Val Ala Phe Leu Ala Tyr Arg Val Asn - 30 -25 Gly Gln Tyr Ile Met Glu Gly Leu Ala Ser Ser Phe Leu Phe Thr Met -20 -15 -10 Gly Gly Leu Gly Phe Ile Ile Leu Asp Gly Ser Asn Ala Pro Asn Ile 5 10 1 Pro Lys Leu Asn Arg Phe Leu Leu Leu Phe Ile Gly Phe Val Cys Val 20 25 Leu Xaa Ser Phe Xaa Xaa Ala Arg Val Phe Met Arg Met Lys Leu Pro 35 Gly Tyr Leu Met Gly

<210> 391 <211> 69 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -49..-1

<210> 392 <211> 241 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -30..-1 <400> 392 Met Gly Thr Ala Ser Arg Ser Asn Ile Ala Arg H.s Leu Gln Thr Asn **-25** -20 Leu Ile Leu Phe Cys Val Gly Ala Val Gly Ala Cys Thr Leu Ser Val -10 Thr Gln Pro Trp Tyr Leu Glu Val Asp Tyr Thr His Glu Ala Val Thr 15 10 5 Ile Lys Cys Thr Phe Ser Ala Thr Gly Cys Pro Ser Glu Gln Pro Thr 25

Cys Leu Trp Phe Arg Tyr Gly Ala His Gln Pro Glu Asn Leu Cys Leu 40 45 Asp Gly Cys Lys Ser Glu Ala Xaa Lys Phe Thr Val Arg Glu Ala Leu 55 60 Lys Glu Asn Gln Val Ser Leu Thr Val Asn Arg Val Thr Ser Asn Asp 70 75 Ser Ala Ile Tyr Ile Cys Gly Ile Ala Phe Pro Ser Val Pro Glu Ala 90 Arg Ala Lys Gln Thr Gly Gly Gly Thr Thr Leu Val Val Arg Glu Ile 105 110 Lys Leu Leu Ser Lys Glu Leu Arg Ser Phe Leu Thr Ala Leu Val Ser 125 120 Leu Leu Ser Val Tyr Val Thr Gly Val Cys Val Ala Phe Ile Leu Leu 135 140 Ser Lys Ser Lys Ser Asn Pro Leu Arg Asn Lys Glu Ile Lys Glu Asp 150 155 160 Ser Gln Lys Lys Lys Ser Ala Arg Arg Ile Phe Gln Glu Ile Ala Gln 170 175 165 Glu Leu Tyr His Lys Arg His Val Glu Thr Asn Gln Gln Ser Glu Lys 185 190 Asp Asn Asn Thr Tyr Glu Asn Arg Arg Val Leu Ser Asn Tyr Glu Arg 205 200 195 Pro

<210> 393 <211> 47 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -30..-1

<210> 394 <211> 65 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -28..-1

25 30 35

Ser

<210> 395

<211> 73

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -24..-1

<400> 395

Met Thr Cys Trp Met Leu Pro Pro Ile Ser Phe Leu Ser Tyr Leu Pro
-20 -15 -10

Leu Trp Leu Gly Pro Ile Trp Pro Cys Ser Gly Ser Thr Leu Gly Lys

Pro Asp Pro Gly Val Trp Pro Ser Leu Phe Arg Pro Trp Asp Ala Ala 10 15 20

Ser Pro Gly Asn Tyr Ala Leu Ser Arg Gly Xaa Asn Xaa Tyr Xaa Xaa 25 30 35 40

Trp Gly Gln Gly Thr His Ser Ser Leu

<210> 396

<211> 60

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -18..-1

<400> 396

Met Pro Cys Pro Thr Trp Thr Cys Leu Lys Ser Phe Pro Ser Pro Thr
-15 -10 -5

Ser Ser His Ala Ser Ser Leu His Leu Pro Pro Ser Cys Thr Arg Leu
1 5 - 10

Thr Leu Thr Gln Thr Leu Arg Thr Gly Met His Leu Ser Arg Ala Leu 15 20 25 30

Gln Gly Thr Leu Thr Arg Leu Gln Ser Thr Pro Ala 35

<210> 397

<211>.192

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -93..-1

<400> 397

Met Ala Glu Leu Gly Leu Asn Glu His His Gln Asn Glu Val Ile Asn
-90 -85 -80

Tyr Met Arg Phe Ala Arg Ser Lys Arg Gly Leu Arg Leu Lys Thr Val

```
- 75
                          -70
Asp Ser Cys Phe Gln Asp Leu Lys Glu Ser Arg Leu Val Glu Asp Thr
                     -55
Phe Thr Ile Asp Glu Val Ser Glu Val Leu Asn Gly Leu Gln Ala Val
               -40
                                  - 35
Val His Ser Glu Val Glu Ser Glu Leu Ile Asn Thr Ala Tyr Thr Asn
             -25
                               -20
Val Leu Leu Arg Gln Leu Phe Ala Gln Ala Glu Lys Trp Tyr Leu
                 -5
          -10
Lys Leu Gln Thr Asp Ile Ser Glu Leu Glu Asn Arg Glu Leu Leu Glu
                    10
                             15
Gln Xaa Ala Glu Phe Glu Lys Ala Xaa Ile Thr Ser Ser Asn Lys Lys
                  25
Pro Ile Leu Xaa Val Thr Xaa Pro Lys Leu Ala Pro Leu Asn Glu Gly
            40
                               45
Gly Thr Ala Lys Leu Leu Asn Lys Val Ile Cys Ile Ile Leu Arg Asn
         .55
                            60
Gly Lys Ser Leu Ile Leu Ser Cys His Cys Leu Gly Trp Arg Asn Lys
                        75
Ser Gly Arg Phe Val Ser Gly Pro Leu Arg Ile Ile Ser Pro Leu Gln
                     90
```

<210> 398 <211> 149 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -72...-1

<400> 398

Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr Ile Ser Ile Phe -65 -60 Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro Ile Gln Ala Leu -50 - 45 Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser Ser Ser Gln Lys -35 -30 Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu Met Gly Leu Ala -15 -20 Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu Pro Thr His Ala -5 1 Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg Met Glu Ser Val 15 20 Val Glu Asp Cys Phe Cys Glu His Glu Lys Ala Ala Pro Gly Pro Tyr 35 30 Val Phe Gly Ser Tyr Leu His Pro Ser Leu Ser Pro Val Ala Pro Gln 45 50 His Thr Leu Lys Leu Ile Thr Tyr Val Lys Lys Asn Gln Lys Thr Leu 60 65 Phe Ser Met Val Gly

<210> 399 <211> 73 <212> PRT <213> Homo sapiens

75

```
<220>
<221> SIGNAL
<222> -20..-1
<400> 399
Met Thr Pro Leu Leu Thr Leu Ile Leu Val Val Leu Met Gly Leu Pro
                    -15
                                       -10
Leu Ala Gln Ala Leu Asp Cys His Val Cys Ala Tyr Asn Gly Asp Asn
                                                   10
Cys Phe Asn Pro Met Arg Cys Pro Ala Met Val Ala Tyr Cys Met Thr
                           20
Thr Arg Thr Tyr Tyr Thr Pro Thr Arg Met Lys Val Ser Lys Ser Cys
                      35
Val Pro Arg Cys Phe Glu Xaa Cys Val
                   50
                          بالجدائعة والمساور
<210> 400
<211> 86
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
Met Asn Leu His Phe Pro Gln Trp Phe Val His Ser Ser Ala Leu Gly
                                       -10
                   -15
Leu Val Leu Ala Pro Pro Phe Ser Ser Pro Gly Thr Asp Pro Thr Phe
                                                    10
Pro Cys Ile Tyr Cys Arg Leu Leu Asn Met Ile Met Thr Arg Leu Ala
                            20
        15
Phe Ser Phe Ile Thr Cys Leu Cys Pro Asn Leu Lys Glu Val Cys Leu
                                           40
                       35
Ile Leu Pro Glu Lys Asn Cys Asn Ser Arg His Ala Gly Phe Val Gly
                                        55
                    50
Pro Xaa Lys Leu Arg Gln
<210> 401
<211> 78
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 401
Met Cys Pro Val Phe Ser Lys Gln Leu Leu Ala Cys Gly Ser Leu Leu
                        -15
                                            -10
 -20
Pro Gly Leu Trp Gln His Leu Thr Ala Asn His Trp Pro Pro Phe Ser
                                    5
Xaa Phe Leu Cys Thr Val Cys Ser Gly Ser Ser Glu Gln Ile Ser Glu
                                20
            15
Tyr Thr Ala Ser Ala Thr Pro Pro Leu Cys Arg Ser Leu Asn Gin Glu
```

30 35 40 Pro Phe Val Ser Arg Ala Ile Arg Pro Lys Tyr Ser Ile Thr

### nformation on pater I family members

F /IB 98/02122

Patent document cited in search report		Publication date		atent family nember(s)	Publication date
WO 9906549	A	11-02-1999	AU	8555098 A	22-02-1999
WO 9634981	A	07-11-1996	FR FR AU CA EP	2733765 A 2733762 A 5982996 A 2220045 A 0824598 A	08-11-1996 08-11-1996 21-11-1996 07-11-1996 25-02-1996
EP 0625572	A	23-11-1994	JP WO US	6153953 A 9408001 A 5597713 A	03-06-1994 14-04-1994 28-01-1997
WO 9707198	Α .	27-02-1997	US AU AU CA CA EP EP WO	5707829 A 6712396 A 6768596 A 2227220 A 2229208 A 0839196 A 0851875 A 9704097 A	13-01-1998 18-02-1997 12-03-1997 06-02-1997 27-02-1997 06-05-1998 08-07-1998 06-02-1997

# FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: Invention 1: Claims 1-20, all partially.

Nucleic acid comprising the sequence as in Seq.ID:40, complementary sequence or fragments, host cell containing said nucleic acid. Polypeptide as in Seq.ID:141, encoded by said polynucleotide, or fragments, method of making said polypeptide. Antibody specifically binding to said polypeptide.

2. Claims: Inventions 2-233: Claims 1-20, all partially, as far as applicable.

Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:41-140, 242-377, and corresponding polypeptides, where invention 2 is limited to Seq.ID:41 and 142, invention 3 is limited to Seq.ID:42 and 143, ...., invention 8 is limited to Seq.ID:47 and 148, invention 9 is limited to Seq.ID:48,49,110,149,150 and 211, invention 10 is limited to Seq.ID:50 and 151, ...., invention 32 is limited to Seq.ID:72 and 173, invention 33 is limited to Seq.ID:73,74,131,174,175 and 232, invention 34 is limited to Seq.ID:75 and 176, ...., invention 233 is limited to Seq.ID:377 and 513.

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

# INTERNATIONAL SEARCH REPORT

international application No.

PCT/IB 98/02122

Box i Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This international Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons.
Claims Nos. Claims
2. Clarms Nos because they relate to parts of the international Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carned out, specifically:
Claims Nos.:  because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box il Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
See additional sheet.
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:
No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.  Invention 1, Claims 1+20 partially.
Remark on Protest  The additional search 'ees were accompanied by the applicant's protest.  No protest accompanied the cayment of additional search fees.

International Application No. 7/18 98/02122

C.(Continu:	ILION) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LOCKHART D.J. ET AL.: "Expression monitoring by hybridization to high-density oligonucleotide arrays" BIO/TECHNOLOGY, no. 14, 14 December 1996 (1996-12-14), pages 1675-1680, XPO02074420 abstract	18
:	·	
	•	
	·	
	·	

Category *	I CANDO AL PAGUMENT WITH INDUSTRIAL WITH CLOSULATED AT THE PROVEST ASSESSES	Relevant to cusm No.
	Citation of document, with indication, where appropriate, of the resevant passages	
A	WO 96 34981 A (GENSET (FR); NICOLAEVNA MERENKOVA I.; DUMAS MILNE EDWARDS JB.G.) 7 November 1996 (1996-11-07) cited in the application abstract	
A	EP 0 625 572 A (KANAGAWA ACAD OF SCIENCE AND TECHNOL FOUNDATION (JP); KATO S; SEKINE S) 23 November 1994 (1994-11-23) cited in the application abstract	
A	CARNINCI P. ET AL.: "High-efficiency full-length cDNA cloning by biotinylated CAP trapper" GENOMICS, vol. 37, no. 3, 1 November 1996 (1996-11-01), pages 327-336, XP002081729 cited in the application abstract	
A	KATO S. ET AL.: "Construction of a human full-length cDNA bank" GENE, vol. 150, 1994, pages 243-250, XP002081364 cited in the application abstract	
A	WO 97 07198 A (GENETICS INSTITUTE INC (US); JACOBS K; MCCOY JM; KELLEHER K; CARLIN M) 27 February 1997 (1997-02-27)	
A	TASHIRO K. ET AL.: "Signal sequence trap: a cloning strategy for secreted proteins and type I membrane proteins" SCIENCE, vol. 261, 30 July 1993 (1993-07-30), pages 600-603, XP000673204 abstract	
A	YOKOYAMA-KOBAYASHI M. ET AL.: "A signal sequence detection system using secreted protease activity as an indicator" GENE, vol. 163, 1995, pages 193-196, XP002053953 abstract	
A	HEIJNE VON G.: "A new method for predicting signal sequence cleavage sites" NUCLEIC ACIDS RESEARCH, vol. 14, no. 11, 1986, pages 4683-4690, XP002053954 cited in the application	

A CLASSIFICATION OF SUBJECT MATTER IPC 6 C12N15/12 C07 CO7K14/47 C07K16/18 C12Q1/68 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12N C07K C12Q Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. E,L WO 99 06549 A (GENSET (FR); DUMAS MILNE 1-20 EDWARDS J.-B.; DUCLERT A.; LACROIX B.) 11 February 1999 (1999-02-11) L: Priority abstract page 6 - page 12 page 129 - page 133; claims Seq. ID: 251 page 213 - page 214 Seq. ID: 484 page 366 - page 367 Х Database EMBL, entry HS695112 2,5,8 Accession number R50695 24 May 1995 95% identity with Seq.ID:40 nt.1-384 XP002097725 the whole document -/--Further documents are listed in the continuation of box C. Х Patent family members are listed in annex. Special categories of cited documents: "I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the *A* document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to myolve an inventive step when the document is taken alone filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-ments, such combination being obvious to a person skilled "O" document referring to an oral disclosure, use, exhibition or other means n the art. *P* document published prior to the international filling date but later than the priority date claimed "3" document member of the same patent family Date of the actual completion of the international search Date of making of the international search report **2** 7. 07. 99 24 March 1999 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk . Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Macchia, G Fax: (+31-70) 340-3016

# FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

A	L	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
A	M	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
	T	Austria	FR	France	LU	Luxembourg	SN	Senegal
	Ú	Australia	GA	Gabon	LV	Larvia	SZ	Swaziland
	Z	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
E	BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
E	3B -	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
E	BE.	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
E	3F	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
	3G	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
I	3,1	Benin	Œ	Ireland	MN	Mongolia	UA	Ukraine
1	3R	Brazil	IL	Israel	MR	Mauritania	UG	Uganda .
E	3Y	Belarus	IS	Iceland	MW	Malawi	US	United States of America
(	CA	Салада	ΙT	Italy	MX	Mexico	UZ	Uzbekistan
(	CF.	Central African Republic	JP	Japan	NE	Niger	VN	Vict Nam
(	CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
	CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
	21	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
	CM	Cameroon		Republic of Korea	PL	Poland		
	CN	China	KR	Republic of Korea	PT	Portugal		
	ะบ	Cuba	KZ	Kazakstan	RO	Romania		
	CZ.	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
	30	Germany	LI	Liechtenstein	SD	Sudan		
	οK	Denmark	LK	Sri Lanka	SR	Sweden		
1	EE	Estonia	1.R	Liberia	SG	Singapore		

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)										
(51) International Patent (	Classification 6:		(11) International Publication Number:	WO 99/31236						
C12N 15/12, C07F 1/68	C 14/47, 16/18, C12Q	A3	(43) International Publication Date:	24 June 1999 (24.06.99)						
(21) International Applicat	ion Number: PCT/II	B98/021	22 (81) Designated States: AL, AM, AT, A BY, CA, CH, CN, CU, CZ, DE							
(22) International Filing D	ate: 17 December 1998		IS, JP, KE, KG, KP, KR,							
(30) Priority Data:			MW, MX, NO, NZ, PL, PT, RC SL, TJ, TM, TR, TT, UA, UC							
60/069,957	17 December 1997 (17.12.9	•	JS ARIPO patent (GH, GM, KE, L.							
60/074,121	9 February 1998 (09.02.98)	) (	JS Eurasian patent (AM, AZ, BY, k	(G, KZ, MD, RU, TJ, TM),						
60/081,563	13 April 1998 (13.04.98)	τ	JS European patent (AT, BE, CH,	CY, DE, DK, ES, FI, FR,						
60/096,116	10 August 1998 (10.08.98)	τ	JS GB, GR, IE, IT, LU, MC, NL,	•						

(71) Applicant (for all designated States except US): GENSET [FR/FR]; 24, rue Royale, F-75008 Paris (FR).

### (72) Inventors; and

- (75) Inventors/Applicants (for US only): BOUGUELERET, Lydie [FR/FR]; 108, avenue Victor Hugo, F-92170 Vanves (FR). DUCLERT, Aymeric [FR/FR]; 6 ter, rue Victorine, F-94100 Saint-Maur (FR). DUMAS MILNE EDWARDS, Jean-Baptiste [FR/FR]; 8, rue Grégoire de Tours, F-75006 Paris (FR).
- (74) Agents: MARTIN, Jean-Jacques et al.; Cabinet Regimbeau, 26, avenue Kléber, F-75116 Paris (FR).

### Published

With international search report.

TD, TG).

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN,

(88) Date of publication of the international search report: 10 September 1999 (10.09.99)

(54) Title: EXTENDED cDNAs FOR SECRETED PROTEINS

### (57) Abstract

The sequences of extended cDNAs encoding secreted proteins are disclosed. The extended cDNAs can be used to express secreted proteins or portions thereof or to obtain antibodies capable of specifically binding to the secreted proteins. The extended cDNAs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. The extended cDNAs may also be used to design expression vectors and secretion vectors.

45

50

55

145

160

175

```
<210> 402
<211> 65
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -28..-1
<400> 402
Met Gly Lys Gly His Gln Arg Pro Trp Trp Lys Val Leu Pro Leu Ser
                              -20
Cys Phe Leu Val Ala Leu Ile Ile Trp Cys Tyr Leu Arg Glu Glu Ser
     -10
                          -5
Glu Ala Asp Gln Trp Leu Arg Gln Val Trp Gly Glu Val Pro Glu Pro
                                      15
                  10
Ser Asp Arg Ser Glu Glu Pro Glu Thr Pro Ala Ala Tyr Arg Ala Arg
              25
Thr
<210> 403
<211> 211
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1
<400> 403
Met Leu Leu Ser Ile Thr Thr Ala Tyr Thr Gly Leu Glu Leu Thr
                           -20
                                              -15
Phe Phe Ser Gly Val Tyr Gly Thr Cys Ile Gly Ala Thr Asn Lys Phe
                       - 5
Gly Ala Glu Glu Xaa Ser Leu Ile Gly Leu Ser Gly Ile Phe Ile Gly
               10
Ile Gly Glu Ile Leu Gly Gly Ser Leu Phe Gly Leu Leu Ser Lys Asn
                               30
Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly. Ile Leu Val His
                           45
Phe Ile Ala Phe Tyr Leu Ile Phe Leu Asn Met Pro Gly Asp Ala Pro
                       60
Ile Ala Pro Val Lys Gly Thr Asp Ser Ser Ala Tyr Ile Lys Ser Ser
                   75
Lys Xaa Phe Ala Ile Leu Cys Xaa Phe Leu Xaa Gly Leu Gly Asn Ser
                                   95
Cys Phe Asn Thr Xaa Leu Leu Xaa Ile Xaa Gly Phe Leu Tyr Ser Glu
                           110
Xaa Ser Ala Pro Xaa Phe Ala Ile Phe Asn Phe Val Gln Ser Ile Cys
                125
      120
Ala Ala Val Ala Phe Phe Tyr Ser Asn Tyr Leu Leu Leu His Trp Gln
```

. 140

155

Leu Leu Val Met Val Ile Phe Gly Phe Xaa Gly Thr Ile Ser Phe Phe

Thr Val Glu Trp Glu Xaa Ala Ala Phe Val Xaa Arg Gly Ser Asp Tyr

```
Arg Ser Ile
```

<210> 404 <2,11> 123 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -80..-1 <400> 404 Met Ser Thr Trp Tyr Leu Ala Leu Asn Lys Ser Tyr Lys Asn Lys Asp -75 -70 Ser Val Arg Ile Tyr Leu Ser Leu Cys Thr Val Ser Ile Lys Phe Thr -60 -55 Tyr Phe His Asp Ile Gln Thr Asn Cys Leu Thr Thr Trp Lys His Ser -45 -40 -35 Arg Cys Arg Phe Tyr Trp Ala Phe Gly Gly Ser Ile Leu Gln His Ser -30 - 25 Val Asp Pro Leu Val Leu Phe Leu Ser Leu Ala Leu Leu Val Thr Pro -15 __-10 -5 Thr Ser Thr Pro Ser Ala Lys Ile Gln Ser Leu Gln Ile Asp Leu Pro 1 5 10 Gly Gly Trp Arg Leu Ala Thr Asp Arg Ile Phe Thr Leu Ser Pro Val 20 25. Pro Met Asp Xaa Pro Leu Ile Leu His Gln Leu 35 40

<210> 405 <211> 86 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -26..-1

<210> 406 <211> 162 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -31..-1
<400> 406
Met Ala Ala Arp Pro Ser Gly Pro Xaa Ala Pro Glu Ala Val Thr
               -25 -20
Ala Arg Leu Val Gly Val Leu Trp Phe Val Ser Val Thr Thr Gly Pro
                  -10
                                  - 5
Trp Gly Ala Val Ala Thr Ser Ala Gly Gly Glu Glu Ser Leu Lys Cys
                      10
                                     15
Glu Asp Leu Lys Val Gly Gln Tyr Ile Cys Lys Asp Pro Lys Ile Asn
                         25
Asp Ala Thr Gln Glu Pro Val Asn Cys Thr Asn Tyr Thr Ala His Val
                     40
                                       45
Ser Cys Phe Pro Ala Pro Asn Ile Thr Cys Lys Asp Ser Ser Gly Asn
               55
                                    60
Glu Thr His Phe Thr Gly Asn Glu Val Gly Phe Phe Lys Pro Ile Ser
Cys Arg Asn Val Asn Gly Tyr Ser Tyr Asn Glu Gln Ser His Val Ser
        85
                            90
Phe Ser Trp Met Val Gly Ser Arg Ser Ile Leu Pro Trp Ile Pro Cys
     100
                       105
                                          110
Phe Gly Phe Val Lys Xaa Xaa His Cys Arg Val Xaa Trp Asn Trp Glu
 115
            . 120
Pro Asn
130
<210> 407
<211> 98
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
<400> 407
Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile
Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe
                      -15
                                        -10
Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu
Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Xaa Gln
        15
                             20
Xaa Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly
                         35
                                           40
Gly Phe Ser Phe Cys Gln Xaa Arg Leu Asn Lys Arg Lys Glu Tyr Met
          . 50
Val Arg
60
```

<210> 408 <211> 70 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -15..-1
<400> 408
Met Arg Phe Leu Pro Cys Cys Leu Leu Trp Ser Val Phe Asn Pro Glu
-15
                  -10
                              - 5
                                                        1
Ser Leu Asn Cys His Tyr Phe Xaa Xaa Glu Xaa Cys Ile Phe Xaa Ser
        5
                            - 10
                                                15
Leu Gln Tyr Tyr Glu Ile Ser Leu Gln Glu Lys Leu Leu Gly Phe Leu
      20
                          25
                                            3.0
Trp Leu Cys Phe Leu Ser Tyr Phe Phe Arg Ala Val Tyr Phe Leu Ile
                                         45
                     40
Asp Phe Ser Ser Phe Thr
50
<210> 409
<211> 60
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -45..-1
<400> 409
Met His Ser Leu Phe Ile Ala Ser Leu Lys Val Leu Phe Tyr Tyr Ser
-45
                   -40
                                     -35
Phe Ser Phe Arg Phe Asn Trp Phe Asp Cys Leu Leu His Asn Leu Gly
                                 -20
                                                   -15
            - -25
Glu Asn Phe Leu Ser Leu Leu Ser Lys Ser Cys Ser Ala Asp Pro Ser
          -10
                              - 5
Gly Ser Thr Phe Met Arg Asp Ile Glu Thr Asn Lys
   5
                       10
<210> 410
<211> 39
<212> PRT -
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1
<400> 410
Met Pro Glu Ala Val Glu Gln Ser Ala His Leu Phe Val Thr Trp Ser
                                          -10
       -20
                          -15
Ser Gln Arg Ala Leu Ser His Pro Ala Pro Phe Leu Thr Xaa Xaa Lys
                                      5
 -5
                      1
Asn Pro Phe Leu Trp Lys Leu
               15
```

<210> 411 <211> 51 <212> PRT

```
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 411
Met Ala Phe Gln Ser Leu Leu Glu Met Lys Phe Phe Leu Cys Ala Ala
        -20
                           -15
Phe Pro Leu Gly Ala Gly Val Lys Met Phe His Tyr Leu Gly Pro Gly
 -5
                     1
                                5
Lys Pro Leu Xaa Gln Ala Ser Pro Ser Pro His Pro His Arg Xaa Arg
10
              15
                                20
Ile Trp Pro
<210> 412
<211> 95
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -48..-1
<400> 412
Met Ala Ser Ser His Trp Asn Glu Thr Thr Thr Ser Val Tyr Gln Tyr
       -45
                         -40
                                   -35
Leu Gly Phe Gln Val Gln Lys Ile Tyr Pro Phe His Asp Asn Trp Asn
      -30
                        -25
                                         -20
Thr Ala Cys Phe Val Ile Leu Leu Leu Phe Ile Phe Thr Val Val Ser
 -15
                    -10 -5
Leu Val Val Leu Ala Phe Leu Tyr Glu Val Leu Xaa Xaa Cys Cys
1 5
                             10
                                              15
Val Lys Asn Lys Thr Val Lys Asp Leu Lys Ser Glu Pro Asn Pro Leu
         20
                          25
Xaa Xaa Met Met Asp Asn Ile Arg Lys Arg Glu Thr Glu Val Val
                        40
<210> 413
<211> 60
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -32..-1
<400> 413
Met Asp Glu Tyr Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly
-30 -25 -20
```

Gln Met Phe Thr Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys
-15
Gln Arg Phe Phe Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser
1 5 10 15
Thr Val Thr Pro Ser Trp Arg Leu Cys Leu Val Ser
20 25

<210> 414

```
<211> 170
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -79..-1
<400> 414
Met Glu Asp Pro Asn Pro Glu Glu Asn Met Lys Gln Gln Asp Ser Pro
                -75
                                    - 70
Lys Glu Arg Ser Pro Gln Ser Pro Gly Gly Asn Ile Cys His Leu Gly
                                 - 55
Ala Pro Lys Cys Thr Arg Cys Leu Ile Thr Phe Ala Asp Ser Lys Phe
                            -40
Gln Glu Arg His Met Lys Arg Glu His Pro Ala Asp Phe Val Ala Gln
                        -25
                                            -20
Lys Leu Gln Gly Val Leu Phe Ile Cys Phe Thr Cys Ala Arg Ser Phe
                    -10
                                        - 5
Pro Ser Ser Lys Ala Xaa Xaa Thr His Gln Arg Ser His Gly Pro Xaa
                               10
Ala Lys Pro Thr Leu Pro Val Ala Thr Thr Thr Ala Gln Pro Thr Phe
                            25
Pro Cys Pro Asp Cys Gly Lys Thr Phe Gly Gln Ala Val Ser Leu Xaa
  35
                        40
Arg His Xaa Gln Xaa His Glu Val Arg Ala Pro Pro Gly Thr Phe Ala
                    55
                                        60
Cys Thr Xaa Cys Gly Gln Asp Phe Ala Gln Glu Xaa Gly Leu His Gln
                70
                                    75
His Tyr Ile Arg His Ala Arg Gly Gly Leu
            85
```

<210> 415 <211> 190 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -82..-1

<400> 415

Met Tyr Val Trp Pro Cys Ala Val Val Leu Ala Gln Tyr Leu Trp Phe -75 - 70 His Arg Arg Ser Leu Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala Gly -60 -55 Val Ser Leu Pro Gly Ile Leu Ala Ala Lys Cys Gly Ala Glu Val Ile -50 -45 -40 Leu Ser Asp Ser Ser Glu Leu Pro His Cys Leu Glu Val Cys Arg Gln -30 -25 -20 Ser Cys Gln Met Asn Asn Leu Pro His Leu Gln Val Val Gly Leu Thr -15 -10 Trp Gly His Ile Ser Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp Ile 1.0 Ile Leu Ala Ser Asp Val Phe Phe Glu Pro Glu Xaa Phe Glu Asp Ile 20 25 Leu Ala Thr Ile Tyr Phe Leu Met His Lys Asn Pro Lys Val Gln Leu Trp Ser Thr Tyr Gln Val Arg Xaa Ala Asp Trp Ser Leu Glu Ala Leu 50 50 55 55 60

Leu Tyr Lys Trp Asp Met Lys Cys Val His Ile Pro Leu Glu Ser Phe 65 70 70 75 75

Asp Ala Asp Lys Glu Xaa Ile Ala Glu Ser Thr Leu Pro Gly Arg His 80 85 5 90 90

Thr Val Glu Met Leu Val Ile Ser Phe Ala Lys Asp Ser Leu 95

<210 > 416 <211 > 114 <212 > PRT <213 > Homo sapiens <220 > <221 > SIGNAL <222 > -60..-1

<400> 416 Met Met Ala Ala Val Pro Pro Gly Leu Glu Pro Trp Asn Arg Val Arg -55 -50 Ile Pro Lys Ala Gly Asn Arg Ser Ala Val Thr Val Gln Asn Pro Gly -40 -35 Ala Ala Leu Asp Leu Cys Ile Ala Ala Val Ile Lys Glu Cys His Leu -25 -20 Val Ile Leu Ser Leu Lys Ser Gln Thr Leu Asp Ala Glu Thr Asp Val -10 -5 1. Leu Cys Ala Val Leu Tyr Ser Asn His Asn Arg Met Gly Arg His Lys 10 15 Pro His Leu Ala Leu Lys Gln Val Glu Gln Cys Leu Lys Arg Leu Lys 25 30 Asn Met Asn Leu Glu Gly Ser Ile Gln Asp Leu Phe Glu Leu Phe Ser Ser Lys

<210> 417 <211> 161 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -108..-1

<400> 417 Met Thr Ser Gly Gln Ala Arg Ala Ser Xaa Gln Ser Pro Gln Ala Leu -105 -100 -95 Glu Asp Ser Gly Pro Val Asn Ile Ser Val Ser Ile Thr Leu Thr Leu -85 -80 Asp Pro Leu Lys Pro Phe Gly Gly Tyr Ser Arg Asn Val Thr His Leu -75 . -70 Tyr Ser Thr Ile Leu Gly His Gln Ile Gly Leu Ser Gly Arg Glu Ala -55 -50 -60 His Glu Glu Ile Asn Ile Thr Phe Thr Leu Pro Thr Ala Trp Ser Ser -40 -35 -30 Asp Asp Cys Ala Leu His Gly His Cys Glu Gln Val Val Phe Thr Ala -20 -15 Cys Met Thr Leu Thr Ala Ser Pro Gly Val Phe Pro Ser Leu Tyr Ser

15 20 25

Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro
30 35 40

Leu Arg Met

Leu Arg Met

<210> 418

<210> 419 <211> 332

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -32..-1

<400> 419

Met Ile Xaa Leu Arg Asp Thr Ala Ala Ser Leu Arg Leu Glu Arg Asp
-30 -25 -20

Thr Arg Gln Leu Pro Leu Leu Thr Ser Ala Leu His Gly Leu Gln Gln
-15 -5

Gln His Pro Ala Phe Ser Gly Val Ala Arg Leu Ala Lys Arg Trp Val 1 5 10 15

Arg Ala Gln Leu Leu Gly Glu Gly Phe Ala Asp Glu Ser Leu Asp Leu 20 25 30

Val Ala Ala Leu Phe Leu His Pro Glu Pro Phe Thr Pro Pro Ser 35 40 45

Ser Pro Gln Val Gly Phe Leu Arg Phe Leu Phe Leu Val Ser Thr Phe 50 60

Asp Trp Lys Asn Asn Pro Leu Phe Val Asn Leu Asn Asn Glu Leu Thr 65 70 75 80

Val Glu Glu Gln Val Glu Ile Arg Ser Gly Phe Leu Ala Ala Arg Ala 85 90 95

Gln Leu Pro Val Mét Val Ile Val Thr Pro Gln Xaa Arg Lys Asn Ser 100 105 110

Val Trp Thr Gln Asp Gly Pro Ser Ala Gln Ile Leú Gln Gln Leu Val 115 120 125 Val Leu Ala Ala Glu Xaa Leu Pro Met Leu Xaa Xaa Gln Leu Met Asp 135 140 Pro Arg Gly Pro Gly Asp Ile Arg Thr Xaa Phe Arg Pro Pro Leu Asp 150 155 Ile Tyr Asp Val Leu Ile Arg Leu Ser Pro Arg His Ile Pro Arg His 165 170 Arg Gln Ala Val Asp Ser Pro Ala Ala Ser Phe Cys Arg Gly Leu Leu 180 185 190 Ser Gln Pro Gly Pro Ser Ser Leu Met Pro Val Leu Gly Xaa Asp Pro 200 205 Pro Gln Leu Tyr Leu Thr Gln Leu Xaa Glu Ala Phe Gly Asp Leu Ala 215 220 Leu Phe Phe Tyr Asp Gln His Gly Glu Val Ile Gly Val Leu Trp 230 235 Lys Pro Thr Ser Phe Gln Pro Gln Pro Phe Lys Ala Ser Ser Thr Lys 245 250 Gly Arg Met Val Met Ser Arg Gly Glu Leu Val Met Val Pro Asn 260 265 Val Glu Ala Ile Leu Glu Asp Phe Ala Val Leu Gly Glu Gly Leu Val 280 Gln Thr Val Glu Ala Arg Ser Glu Arg Trp Thr Val 295

<210> 420 <211> 65 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<400> 420

<222> -19..-1

Met Gly Gly Ile Trp Asn Ala Leu Ser Met Ser Ser Phe Ser Phe His
-15 - 16 - 10 - 5 - 5

Ser Ser Ser Cys Ser Ala Leu Ser Ala Lys Ser Leu Leu Ser Arg His
1 - 5 - 10 - 10

His Ile Leu Gln Gln Phe Leu Val Arg Lys Ser Val Pro Leu Glu Asn
15 - 20 - 25

Ala Ser Leu Pro Phe Pro His Leu Gly Ser Ser Leu Phe Lys Ile Val
30 - 35 - 40 - 45

Gly

<210> 421 <211> 57 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -30..-1

Met Pro Thr Gly Lys Gln Leu Ala Asp Ile Gly Tyr Lys Thr Phe Ser
-30 -25 -20 -15
Thr Ser Met Met Leu Leu Thr Val Tyr Gly Gly Tyr Leu Cys Ser Val

```
- 5
Arg Val Tyr His Tyr Phe Gln Trp Arg Arg Ala Gln Arg Gln Ala Ala
                        10
Glu Glu Gln Lys Xaa Ser Gly Ile Met
                       25
   20
```

<210> 422 <211> 85 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -17..-1

<400> 422

65

Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val -15 -10 Gly Phe Pro Val Ser Gln Asp Gln Glu Arg Glu Lys Arg Ser Ile Ser 1 10 Asp Ser Asp Glu Leu Ala Ser Gly Xaa Phe Val Phe Pro Tyr Pro Tyr 25 Pro Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe 35 40 Arg Arg Asn Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Thr Thr Pro 55 Leu Pro Ser Glu Lys

<210> 423 <211> 85 <212> PRT <213> Homo sapiens

<220> <221> SIGNAL <222> -17..-1

<400> 423

Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val . -15 -10 Gly Phe Pro Val Ser Gln Asp Xaa Glu Arg Glu Lys Arg Ser Ile Ser 10 Asp Ser Asp Glu Leu Ala Ser Gly Phe Phe Val Phe Pro Tyr Pro Tyr 25 Pro Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe 35 40 Arg Arg Asn Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Thr Thr Pro 55 50 Leu Pro Ser Glu Lys 65

<210> 424 <211> 69 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -29..-1
<400> 424
Met Thr Cys Arg Gly Ser Cys Ser Tyr Ala Thr Arg Arg Ser Pro Ser
           -25 -20 -15
Glu Leu Ser Leu Leu Pro Ser Ser Leu Trp Val Leu Ala Thr Ser Ser
         -10 -5
Pro Thr Ile Thr Ile Ala Leu Ala Met Ala Ala Gly Asn Leu Cys Pro
                  10
                         15
Leu Pro Ser Ser Xaa Arg Xaa Lys Arg Arg Trp Cys Gln Ala Xaa Gln
                                30
Gln Xaa Ala Leu Leu
            4.0
<210> 425
<211> 122
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -56..-1
<400> 425
Met Val Pro Trp Pro Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Ile
 -55 -50 -45
Ser Arg Phe Pro Phe Leu Pro Thr His Asp Pro Pro Thr Pro Ala His
               -35
                                 -30
-40
Trp Ser Pro Ala Ser His Gln Gln Phe Lys His Xaa Ser Pro Leu Leu
                              -15
                                   -10
             -20
Thr Leu Ala Leu Leu Gly Gln Cys Ser Leu Phe Xaa Asn Leu Arg Lys
                           1 5
Lys Leu Ala Gly Gln Lys Ala Lys Lys Leu Pro Ser Phe Ser Ser Leu
                    15
                                    2.0
Pro Leu Thr Leu Trp Pro Leu Thr Pro Gln Phe Ala Glu Leu Thr Thr
                30
                         35
Val Ala Gln Lys Lys Leu Arg Trp Ser Gly Thr Leu Gly Trp Gly Pro
                                   . 55
                              50
             45
Val Pro Ser Trp Val Gln Phe Phe Leu Gly
          60
<210> 426
<211> 41
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -30..-1
<400> 426
Met Ala Cys Glu Thr His Gly Val Leu Val Pro Ala His Leu Ser Gly
```

Leu Ile Thr Cys Leu Leu Ala Phe Trp Val Pro Ala Ser Cys Ile Gln

- 5

-30 . -25

-20 -15

```
Arg Cys Ser Gly Ser Pro Leu Pro Leu 5 . 10
```

<210> 427
<211> 50
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -36..-1

<210> 428 <211> 136 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -18..-1

<400> 428 Met Asp Ser Leu Arg Lys Met Leu Ile Ser Val Ala Met Leu Gly Ala -10 -15 Xaa Ala Gly Val Gly Tyr Ala Leu Leu Val Ile Val Thr Pro Gly Glu 10 Arg Arg Lys Gln Glu Met Leu Lys Glu Met Pro Leu Gln Asp Pro Arg 25 20 Ser Arg Glu Glu Ala Ala Arg Thr Gln Gln Leu Leu Leu Ala Thr Leu 40 35 Gln Glu Ala Ala Thr Thr Gln Glu Asn Val Ala Trp Arg Lys Asn Trp Met Val Gly Gly Glu Gly Gly Ala Thr Gly Xaa His Arg Glu Thr Gly 70 Leu Ala Ser Val Gly Ala Gly Pro Trp Leu Gly Arg Arg Asn Pro Arg 85 Gln Leu Ser Pro Ser Trp Ala Xaa Arg Lys Ile Arg Xaa Glu Asn Xaa 100 Met Pro Gly Leu Ser Gly Val Leu 115

<210> 429 <211> 194 <212> PRT <213> Homo sapiens

<220>

<221> SIGNAL <222> -65..-1

<400> 429 Met Gln Asp Ala Pro Leu Ser Cys Leu Ser Pro Thr Lys Trp Ser Ser -60 -55 Val Ser Ser Ala Asp Ser Thr Glu Lys Ser Ala Ser Ala Ala Gly Thr -45 Arg Asn Leu Pro Phe Gln Phe Cys Leu Arg Gln Ala Leu Arg Met Lys -30 -25 -20 Ala Ala Gly Ile Leu Thr Leu Ile Gly Cys Leu Val Thr Gly Val Glu -10 - 5 Ser Lys Ile Tyr Thr Arg Cys Lys Leu Ala Lys Ile Phe Ser Arg Ala Gly Leu Asp Asn Xaa Arg Gly Phe Ser Leu Gly Asn Trp Ile Cys Met 20 25 Ala Tyr Tyr Glu Ser Gly Tyr Asn Thr Thr Ala Gln Thr Val Leu Asp 35 40 Asp Gly Ser Ile Asp Tyr Gly Ile Phe Gln Ile Asn Ser Phe Ala Trp -55 Cys Arg Arg Gly Lys Leu Lys Glu Asn Asn His Cys His Val Ala Cys 75 70 Ser Ala Leu Xaa Thr Asp Asp Leu Thr Asp Ala Ile Ile Cys Ala Xaa 85 90 Lys Ile Val Lys Glu Thr Gln Gly Met Asn Tyr Trp Gln Gly Trp Lys 100 105 Lys His Cys Glu Gly Arg Asp Leu Ser Xaa Trp Lys Lys Gly Cys Glu Val Ser

<210> 430 <211> 141 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -69..-1

<400> 430

Met Thr Ser Gln Pro Val Pro Asn Glu Thr Ile Ile Val Leu Pro Ser -65 -60 Asn Val Ile Asn Phe Ser Gln Ala Glu Lys Pro Glu Pro Thr Asn Gln -45 Gly Gln Asp Ser Leu Lys Lys His Leu His Ala Glu Ile Lys Val Ile -30 Gly Thr Ile Gln Ile Leu Cys Gly Met Met Val Leu Ser Leu Gly Ile -15 -10 Ile Leu Ala Ser Ala Ser Phe Ser Pro Asn Phe Thr Gln Val Thr Ser 1 5 Thr Leu Leu Asn Ser Ala Tyr Pro Phe Ile Gly Pro Phe Phe Val Xaa 20 15 Lys Xaa Ser Glu Glu Gly Arg Met Gly Gln Xaa Gly Glu Glu Xaa Xaa 35 Asn Ser Leu Asn Phe Pro Xaa Ala Ser Leu Leu Xaa Leu Ile Cys Gln Xaa Gln Gly Phe Asn Gly Glu Ser Cys Ser Pro Val Gly

```
<210> 431
<211> 248
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -69..-1
<400> 431
Met Thr Ser Gln Pro Val Pro Asn Glu Thr Ile Ile Val Leu Pro Ser
                -65
Asn Val Ile Asn Phe Ser Gln Ala Glu Lys Pro Glu Pro Thr Asn Gln
           -50
                               -45
Gly Gln Asp Ser Leu Lys Lys His Leu His Ala Glu Xaa Lys Val Ile
                           -30
Gly Thr Ile Gln Ile Leu Cys Gly Met Met Val Leu Ser Leu Gly Ile.
                       -15
                                           -10
Ile Leu Ala Ser Ala Ser Phe Ser Pro Asn Phe Thr Gln Val Thr Ser
- 5
                  1
Thr Leu Leu Asn Ser Ala Tyr Pro Phe Ile Gly Pro Phe Phe Phe Ile
                               20
           15
Ile Ser Gly Ser Leu Ser Ile Ala Thr Lys Lys Arg Leu Thr Asn Leu
       30
                           35
Leu Val His Thr Thr Leu Val Gly Ser Ile Leu Ser Ala Leu Ser Ala
                        50
                                            55
Leu Val Gly Phe Ile Xaa Leu Ser Val Lys Gln Ala Thr Leu Asn Pro
                                        70
Ala Ser Leu Xaa Cys Glu Leu Xaa Lys Asn Asn Ile Pro Thr Xaa Xaa
                                   85
                80
Tyr Val Xaa Tyr Phe Tyr His Asp Ser Leu Tyr Thr Thr Asp Xaa Tyr
                               100
Thr Ala Lys Ala Xaa Leu Ala Gly Thr Leu Ser Leu Met Leu Ile Cys
                            115
                                                120
Thr Leu Leu Glu Phe Cys Xaa Xaa Val Leu Thr Ala Val Leu Arg Trp
                       130
                                           135
Lys Gln Ala Tyr Ser Asp Phe Pro Gly Ser Val Leu Phe Leu Pro Xaa
                                       150
                   145
Ser Tyr Ile Gly Asn Ser Gly Met Ser Ser Lys Met Thr His Asp Cys
               160
                                    165
Gly Tyr Glu Glu Leu Leu Thr Ser
            175
```

```
<210> 432
<211> 49
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -36..-1
<400> 432
Met Gln Val Pro His Leu Arg Val Trp Thr Gln Val Xaa Asp Thr Phe
   -35
                       -30
                                           - 25
Ile Gly Tyr Arg Asn Leu Gly Phe Thr Ser Met Cys Ile Leu Phe His
                                   -10
                   -15
Cys Leu Leu Ser Phe Gln Val Phe Lys Lys Lys Arg Lys Leu Xaa Leu
```

Phe

<210> 433

<211> 86 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -14..-1 <400> 433 Met Val Ala Leu Asn Leu Ile Leu Val Pro Cys Cys Ala Ala Trp Cys -10 - 5 Asp Pro Arg Arg Ile His Ser Gln Asp Asp Val Leu Arg Ser Ser Ala 10 Ala Asp Thr Gly Ser Ala Met Gln Arg Arg Glu Ala Trp Ala Gly Trp 25 Arg Arg Ser Gln Pro Phe Ser Val Gly Leu Pro Ser Ala Glu Arg Leu 45 40 Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg Ser Leu Val Gly Glu Gly 55 His Arg Ile Cys Asp Leu 70

<210> 434 <211> 144 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -58..-1

<400> 434 Met Thr Arg Leu Cys Leu Pro Arg Pro Glu Ala Arg Glu Asp Pro Ile -55 Pro Val Pro Pro Arg Gly Leu Gly Ala Gly Glu Gly Ser Gly Ser Pro -35 Val Arg Pro Pro Val Ser Thr Trp Gly Pro Ser Trp Ala Gln Leu Leu -20 - 15 Asp Ser Val Leu Trp Leu Gly Ala Leu Gly Leu Thr Ile Gln Ala Val - 5 1 Phe Ser Thr Thr Gly Pro Ala Leu Leu Leu Leu Leu Val Ser Phe Leu 15 10 Thr Phe Asp Leu Leu His Arg Pro Ala Val Thr Leu Cys His Ser Ala Asn Phe Ser Pro Gly Ala Arg Val Arg Gly Pro Val Lys Val Leu Asp 45 50 Ser Arg Arg Leu Tyr Ser Cys Lys Trp Val Gln Ser Gln Asp Asn Leu 65 60 Ala Ser Arg Lys His Cys Cys Cys Cys Ser Trp Gly Trp Ala Arg Ser

<210> 435 <211> 121

<210> 436

```
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16...-1
<400> 435
Met Glu Arq Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala
                        -10
                                            - 5
Ser Ala Gly Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln
                                  - 10
Cys Phe Lys Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser
           20
                                25
Pro Leu Asp Gln Val Cys Ile Ser Asn Glu Val Val Val Ser Phe Ser
                             40
Glu Ser Pro Pro Gly Arg Gly Xaa Val Pro Xaa Ala Gly Glu Xaa Pro
                        55
Val Pro Pro Pro Leu Xaa Asp Leu Xaa Met Thr Pro Arg Xaa Xaa Arg
                                        75
Ala Trp Gly Pro Val Gly Pro Lys Val Pro Pro Ala Val Ser Pro Ala
                85
                                    90
Leu Gly Ser Gly Glu His Pro Xaa Xaa
           100
```

<211> 162 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -16..-1 <400> 436 Met Glu Arg Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala -10 Ser Ala Gly Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln Cys Phe Lys Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser 25 Pro Leu Asp Gln Val Cys Ile Ser Asn Glu Val Val Ser Phe Lys 40 Trp Ser Val Arg Val Leu Leu Ser Lys Arg Cys Ala Pro Arg Cys Pro 55 60 Asn Asp Asn Met Xaa Phe Glu Trp Ser Pro Ala Pro Met Val Gln Gly 70 75 Val Ile Thr Arg Arg Cys Cys Ser Trp Ala Leu Cys Asn Arg Ala Leu 85 Thr Pro Gln Glu Gly Arg Trp Ala Leu Xaa Gly Gly Leu Leu Leu Gln 105 Asp Pro Ser Arg Gly Xaa Lys Thr Trp Val Arg Pro Gln Leu Gly Leu 125 120 Pro Leu Cys Leu Pro Xaa Ser Asn Pro Leu Cys Pro Xaa Glu Thr Gln 135 130 Glu Gly 145

<400> 439

-20

```
<210> 437
<211> 110
<212> PRT
<213 > Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 437
Met Xaa Leu Met Val Leu Val Phe Thr Ile Gly Leu Thr Leu Leu Leu
-20 -15 -10
Gly Xaa Gln Ala Met Pro Ala Asn Arg Leu Ser Cys Tyr Arg Lys Ile
Leu Lys Asp His Asn Cys His Asn Leu Pro Glu Gly Val Ala Asp Leu
 15
                        20
Thr Gln Ile Asp Val Asn Val Gln Asp His Phe Trp Asp Gly Lys Gly
              35 . 40
Cys Glu Met Ile Cys Tyr Cys Asn Phe Lys Arg Ile Ala Leu Leu Pro
45
               50
                         55
Lys Arg Arg Phe Leu Trp Thr Lys Asp Leu Phe Arg Asp Ser Leu Gln
                      70
Gln Ser Met Arg Ile Phe Met Tyr Ser Gly Glu His His Ser
<210> 438
<211> 71
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
Met Lys Leu Leu Thr His Asn Leu Leu Ser Ser His Val Arg Gly Val
-15 -10 -5
Gly Ser Arg Gly Phe Pro Leu Arg Leu Gln Ala Thr Glu Val Arg Ile
                           10
Cys Pro Val Glu Phe Asn Pro Asn Phe Val Ala Arg Met Ile Pro Lys
  20 25
                                         30
Val Glu Trp Ser Ala Phe Leu Glu Ala Xaa Asp Asn Leu Arg Leu Ile
                    40
Gln Val Pro Arg Arg Ala Gly
50
<210> 439
<211> 99
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
```

Met Lys Ser Ala Lys Leu Gly Phe Leu Leu Arg Phe Phe Ile Phe Cys

```
<210> 440
<211> 169
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 440
Met Arg Lys Pro Ala Ala Gly Phe Leu Pro Ser Leu Leu Lys Val Leu
-25
                    -20
                                        -15
Leu Leu Pro Leu Ala Pro Ala Ala Gln Asp Ser Thr Gln Ala Ser
                - 5
Thr Pro Gly Ser Pro Leu Ser Pro Thr Glu Tyr Gln Arg Phe Phe Ala
                            15
Leu Leu Thr Pro Thr Trp Lys Ala Glu Thr Thr Cys Arg Leu Arg Ala
                        30
                                            35
Thr His Gly Cys Arg Asn Pro Thr Leu Val Gln Leu Asp Gln Tyr Glu
                    45
                                        50
Asn His Gly Leu Val Pro Asp Gly Ala Val Cys Ser Asn Leu Pro Tyr
                60
                                    65
Ala Ser Trp Phe Glu Ser Phe Cys Gln Phe Thr His Tyr Arg Cys Ser
Asn His Val Tyr Tyr Ala Lys Arg Val Leu Cys Ser Gln Pro Val Ser
Ile Leu Ser Pro Asn Thr Leu Lys Glu Ile Glu Xaa Ser Ala Glu Val
                        110
                                            115
Ser Pro Thr Thr Asp Asp Leu Pro His Leu Thr Pro Leu His Ser Asp
                    125
                                        130
Arg Thr Pro Asp Leu Pro Ala Leu Ala
                140
```

Ala Asp Cys Gly Thr Ile Leu Leu Gln Asp Lys Gln Arg Lys Ile Tyr -55 Cys Val Ala Cys Gln Glu Leu Asp Ser Asp Val Asp Lys Asp Asn Pro -40 - 35 Ala Leu Asn Ala Gln Ala Ala Leu Ser Gln Ala Arg Glu His Gln Leu -20 -15 Ala Ser Ala Ser Glu Leu Pro Leu Gly Ser Arg Pro Ala Pro Gln Pro Pro Val Pro Arg Pro Glu His Cys Glu Gly Ala Ala Ala Gly Leu Lys 10 15 Ala Ala Gln Gly Pro Pro Ala Pro Ala Val Pro Pro Asn Thr Xaa Val 30 25 Met Ala Cys Thr Gln Thr Ala Leu Leu Gln Lys Leu Thr Trp Ala Ser Ala Glu Leu Gly Ser Xaa Thr Ser Xaa Gly Lys Xaa Ala Ser Ser Cys 60 Val Ala Leu Ser Ala His Val Arg Arg Pro Cys Ala Ala Cys Ser Ser Tyr Ser Thr Lys Arg Ser Pro 85

<210> 442 <211> 70 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -15..-1

Val Gly Ala Asn Xaa Leu Cys Leu Gly Met Ala Leu Cys Pro Arg Gln
-15 -10 -5

Ala Thr Arg Ile Pro Leu Asn Gly Thr Trp Leu Phe Thr Pro Val Ser
1 5 10 15

```
Lys Met Ala Thr Val Lys Ser Glu Leu Ile Glu Arg Phe Thr Ser Glu
                                    25
Lys Pro Val His His Ser Lys Val Ser Ile Ile Gly Thr Gly Ser Val
                                40
Gly Met Ala Cys Ala Ile Ser Ile Leu Leu Lys Gly Leu Ser Asp Glu
                            55
Leu Ala Leu Val Asp Leu Asp Glu Xaa Lys Leu Lys Gly Glu Thr Met
                        70
Asp Leu Gln His Gly Ser Pro Phe Thr Lys Met Pro Asn Ile Val Cys
Ser Lys Xaa Tyr Phe Val Thr Ala Asn Ser Asn Leu Val Ile Ile Thr
                                   105
Ala Gly Ala Arg Gln Xaa Lys Gly Glu Thr Arg Leu Asn Leu Xaa Gln
                               120
Arg Asn Val Ala Ile Phe Lys Leu Met Ile Ser Ser Ile Val Gln Tyr
                           135
Ser Pro His Cys Lys Leu Ile Ile Val Ser Asn Pro Val Asp Ile Leu
                       150
                                          155
Thr Tyr Val Ala Trp Lys Leu Ser Ala Phe Pro Lys Asn Arg Ile Ile
                                       170
                   165
Gly Ser Gly Cys Asn Leu Ile Xaa Ala Arg Phe Arg Phe Leu Ile Gly
               180
                                    185
Gln Lys Leu Gly Ile His Ser Glu Ser Cys His Gly Trp Ile Leu Gly
            195
                                200
Glu His Gly Asp Ser Ser Val Pro Val Trp Ser Gly Val Asn Ile Ala
                                                220
       210
                            215
Gly Val Pro Leu Lys Asp Leu Asn Ser Asp Ile Gly Thr Asp Lys Asp
                        230
                                            235
Pro Glu Gln Trp Lys Asn Val His Lys Glu Val Thr Ala Thr Ala Tyr
                   245
                                        250
Glu Ile Ile Lys Met Lys Gly Tyr Thr Ser Trp Ala Ile Gly Leu Ser
                                    265
               260
Val Ala Asp Leu Thr Glu Ser Ile Leu Lys Asn Leu Arg Arg Ile His
                                280
            275
Pro Val Ser Thr Ile Thr Lys Gly Leu Tyr Gly Ile Xaa Glu Glu Val
       290
                            295
Phe Leu Ser Ile Pro Cys Ile Leu Gly Glu Asn Gly Ile Thr Asn Leu
                       310
                                           315
Ile Lys Ile Lys Leu Thr Pro Glu Glu Glu Ala His Leu Lys Lys Ser
                                        330
                   325
Ala Lys Thr Leu Trp Glu Ile Gln Asn Lys Leu Lys Leu
                340
```

```
<210> 444
<211> 39
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -14...1
```

```
<210> 445
  <211> 50
  <212> PRT
  <213> Homo sapiens
  <220>
  <221> SIGNAL
  <222> -37..-1
  <400> 445
  Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val Asn
                            -30 -25
      -35
  Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala Leu
                      -15
                                 -10
  Ser Pro Cys Leu Thr Ala Pro Lys Ser Pro Arg Leu Ala Met Met Pro
                                   5
  Asp Asn
<210> 446
  <211> 51
  <212> PRT
  <213> Homo sapiens
  <220>
  <221> SIGNAL
  <222> -26..-1
  <400> 446
  Met Thr Pro Trp Cys Leu Ala Cys Leu Gly Arg Arg Pro Leu Ala Ser
                        -20
                                           -15
  Leu Gln Trp Ser Leu Thr Leu Ala Trp Cys Gly Ser Gly Ser His Trp
  -10
                    - 5
                                      1
  Thr Glu Arg Pro Xaa Gln Xaa Ser Pro Trp Xaa Ser Leu Ser Ala Thr
                             15
     10
  Thr Arg Gly
         25
  <210> 447
  <211> 242
  <212> PRT
  <213> Homo sapiens
  <220>
  <221> SIGNAL
  <222> -30..-1
  Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His Leu Leu Val
                                       - 2 C
  -30
                     - 25
  Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala Ala Ala Pro
                -10
                                    - 5
  Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu Thr Gly Leu
                                               15
                            10
  Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys Gly Asn Leu
                        25
                                           3.0
  Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp Phe Arg Gly
```

```
35
                                        4.5
Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His Gln Leu Gly
                                    60
Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Met Thr Asp Asn
Lys Thr Gly Glu Val Leu Ile Ser Glu Asn Val Val Ala Ser Ile Gln
                           90
Pro Xaa Glu Gly Xaa Phe Glu Gly Asp Leu Lys Val Pro Arg Met Glu
                       105
                                           110
Glu Lys Glu Ala Leu Val Pro Xaa Gln Lys Ala Thr Asp Ser Phe His
                  120
                                       125
Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile Lys Leu Pro Arg
                135
                                   140
Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His Trp Leu Xaa Glu
            150
                               155
Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu Arg Lys Gly Thr
        165
                           170
                                               175
His Lys Asp Xaa Leu Xaa Xaa Gly Thr Glu Ser Ser His Ser Arg
                       185
                                           190
Leu Ser Pro Arg Lys Xaa His Leu Leu Tyr Ile Leu Xaa Pro Ser Arg
195
                    200
                                       205
Gln Leu
```

<210> 448 <211> 154 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -60..-1

<400> 448 Met Gly Ser Lys Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu -55 Arg Gln Arg Arg Gln Lys Leu Leu Ala Gln Leu His His Arg Lys -40 -35 -30 Arg Val Lys Ala Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu -25 -20 -15 Val Arg Arg Thr Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln - 5 Cys Trp Trp Arg Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln 15 Ala Leu Leu Gly Val Tyr Val Ile Gln Glu Gln Ala Ala Val Lys Leu 25 30 Gln Ser Cys Ile Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met 45 Cys Asn Ala Leu Cys Leu Phe Gln Val Pro Lys Ser Ser Leu Ala Phe 60

Gln Thr Asp Gly Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln

Pro Glu Phe His Ile Glu Ile Leu Ser Ile 85 90

<210> 449 <211> 89 <212> PRT <213> Homo sapiens <220>

. 1

```
<221> SIGNAL
<222> -61..-1
<400> 449
Met Asn Ala Ala Ile Asn Thr Gly Pro Ala Pro Ala Val Thr Lys Thr
             -55
                          -50
Glu Thr Glu Val Gln Asn Pro Asp Val Leu Trp Asp Leu Asp Ile Pro
              -40
                               -35
Glu Ala Arg Ser His Ala Asp Gln Asp Ser Asn Pro Lys Ala Glu Ala
          -25 -20 -15
Leu Leu Pro Cys Asn Leu His Cys Ser Trp Leu His Ser Ser Pro Arg
        -10 -5
Pro Asp Pro His Ser His Phe Pro Ser Xaa Arg Arg Cys Pro Leu Pro
 5 10
                             15
His Pro Cys Ala Thr Tyr Pro Pro Xaa
20 25
<210> 450
<211> 73
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
<400> 450
Met Arg Met Ser Leu Ala Gln Arg Val Leu Leu Thr Trp Leu Phe Thr
                          -15
 -25 -20
Leu Leu Phe Leu Ile Met Leu Val Leu Lys Leu Asp Glu Lys Ala Pro
-10 -5
                               1
Trp Asn Trp Phe Leu Ile Phe Ile Pro Val Trp Ile Phe Asp Thr Ile
        10
                        15
                                      20
Leu Leu Val Leu Leu Ile Val Lys Met Ala Gly Arg Cys Lys Ser Gly
25
                   30
                                      35
Phe Asp Leu Asp Met Asp His Thr Ile
 40
<210> 451
<211> 54
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -34..-1
<400> 451
Met Ile Pro Leu Ile Ser His Leu Ala Glu Ala Ala Pro Pro Thr Ser
          -30 -25 . -20
Trp Ser Leu Ile Ser Ser Val Leu Asn Val Gly His Leu Leu Phe Ser
                       -10
       -15
Ser Ala Cys Ser Val Ser Leu Glu Ala Leu Ser Thr Arg Asn Ile Lys
   1 5
Ala Ile Ile Leu Met Lys
             20
```

```
<210> 452
<211> 121
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -38..-1
<400> 452
Met Glu Ser Pro Gln Leu His Cys Ile Leu Asn Ser Asn Ser Val Ala
           - 3 5
                                -30
Cys Ser Phe Ala Val Gly Ala Gly Phe Leu Ala Phe Leu Ser Cys Leu
                          -15
                                                -10
Ala Phe Leu Val Leu Asp Thr Gln Glu Thr Arg Ile Ala Gly Thr Arg
Phe Lys Thr Ala Phe Gln Leu Leu Asp Phe Ile Leu Ala Val Leu Trp
                15
                                    20
Ala Val Val Trp Phe Met Gly Phe Cys Phe Leu Ala Asn Gln Trp Gln
                                35
His Ser Pro Pro Lys Glu Xaa Leu Leu Gly Ser Ser Ser Ala Gln Ala
                            50
Ala Ile Gly Xaa His Leu Leu His Pro Cys Leu Asp Ile Pro Xaa
                       65
Leu Pro Gly Xaa Pro Gly Pro Pro Lys
                            * 4868 ···
```

<210> 453 <211> 166 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -37..-1

<400> 453 Met Ser Thr Val Gly Leu Phe His Phe Pro Thr Pro Leu Thr Arg Ile -30 Cys Pro Ala Pro Trp Gly Leu Arg Leu Trp Glu Lys Leu Thr Leu Leu -20 -15 -10 Ser Pro Gly Ile Ala Val Thr Pro Val Gln Met Ala Gly Lys Lys Asp Tyr Pro Ala Leu Leu Ser Leu Asp Glu Asn Glu Leu Glu Glu Gln Phe 20 Val Lys Gly His Gly Pro Gly Gly Gln Ala Thr Asn Lys Thr Ser Asn 35 Cys Val Val Leu Lys Xaa Ile Pro Ser Gly Ile Val Val Lys Cys His 50 Gln Thr Arg Ser Val Asp Gln Asn Arg Lys Leu Ala Arg Lys Ile Leu 65 Gln Glu Lys Val Xaa Val Phe Tyr Asn Gly Glu Asn Ser Pro Val His 85 Lys Glu Lys Arg Glu Ala Ala Lys Lys Gin Glu Arg Lys Lys Arg 100 105 Ala Lys Glu Thr Leu Glu Lys Lys Xaa Leu Leu Lys Xaa Leu Trp Glu 115

Ser Ser Lys Lys Val His 125

<210> 454 <211> 180 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -26..-1 <400> 454 Met Gly Ile Gln Thr Ser Pro Val Leu Leu Ala Ser Leu Gly Val Gly -25 -20 Leu Val Thr Leu Leu Gly Leu Ala Val Gly Ser Tyr Leu Val Arg Arg -10 -5 1 Ser Arg Arg Pro Gln Val Thr Leu Leu Asp Pro Asn Glu Lys Tyr Leu 15 Leu Arg Leu Leu Asp Lys Thr Thr Val Ser His Asn Thr Lys Arg Phe 30 35 Arg Phe Ala Leu Pro Thr Ala His His Thr Leu Gly Leu Pro Val Gly 45 Lys His Ile Tyr Leu Ser Thr Arg Ile Asp Gly Ser Leu Val Ile Arg Pro Tyr Thr Pro Val Thr Ser Asp Glu Asp Gln Gly Tyr Val Asp Leu 75 80 Val Xaa Lys Val Tyr Leu Lys Gly Val His Pro Lys Phe Pro Glu Gly 95 Gly Lys Met Ser Xaa Tyr Leu Asp Xaa Leu Lys Val Gly Asp Xaa Val 110 Glu Phe Xaa Gly Pro Ser Gly Leu Leu Thr Tyr Thr Gly Lys Gly His 125 130 Phe Asn Ile Gln Pro Asn Lys Asn Leu His Gln Asn Pro Glu Trp Arg

<210> 455 <211> 91 <212> PRT <213> Homo sapiens

Arg Asn Trp Glu

<220>
<221> SIGNAL
<222> -64..-1

<400> 455 Met Thr Pro Arg Ile Leu Ser Glu Val Gln Phe Ser Ala Phe Cys Pro -55 -60 Tyr Trp Thr Ile Ala Arg Ile Leu Glu Arg Val Gly Ser Ala Cys Phe -45 Arg Leu Glu Leu Cys Ala Ala Ile Val Gly Tyr Phe Val Leu Asp Val -25 -20 Arg Thr Phe Leu Phe Ile Val Val Cys Val Ile Cys Val Thr Leu Asn -5 -15 -10 Phe Pro Arg Phe Tyr Phe Leu Cys Leu Ser Ser Leu Thr Ala Phe Gly 10 Thr Pro Pro Ile Gly Val His Ile Pro Ser Pro

25

20

```
<210> 456
<211> 257
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 456
Met Arg Arg Ile Ser Leu Thr Ser Ser Pro Val Arg Leu Leu Lau Xaa
          -20
                            -15
Leu Leu Leu Leu Ile Ala Leu Glu Ile Met Val Gly Gly His Ser
Leu Cys Phe Asn Phe Thr Ile Lys Ser Leu Ser Arg Pro Gly Gln Pro
                  15
                                      20
Trp Cys Glu Ala His Val Phe Leu Asn Lys Asn Leu Phe Leu Gln Tyr
               30
                                   35
Asn Ser Asp Asn Asn Met Val Lys Pro Leu Gly Leu Leu Gly Lys Lys
                              50
Val Tyr Ala Thr Ser Thr Trp Gly Glu Leu Thr Gln Thr Leu Gly Glu
                          65
Val Gly Arg Asp Leu Arg Met Leu Leu Cys Asp Ile Lys Pro Gln Ile
                     80
Lys Thr Ser Asp Pro Ser Thr Leu Gln Val Xaa Xaa Phe Cys Gln Arg
                  95
                                      100
Glu Ala Glu Arg Cys Thr Gly Ala Ser Trp Gln Phe Ala Thr Asn Gly
                                   115
               110
Glu Lys Ser Leu Leu Phe Asp Ala Met Asn Met Thr Trp Thr Val Ile
                               130
           125
Asn His Glu Ala Ser Xaa Ile Lys Glu Thr Trp Lys Lys Asp Arg Xaa
                           145
Leu Glu Xaa Tyr Phe Arg Lys Leu Ser Lys Gly Asp Cys Asp His Trp
                       160
                                          165
Leu Arg Glu Phe Leu Gly His Trp Glu Ala Met Pro Xaa Pro Xaa Val
                  175
                                      180
Ser Pro Xaa Asn Ala Ser Xaa Ile His Trp Ser Ser Ser Xaa Leu Pro
              190
                                   195
Xaa Xaa Trp Ile Ile Leu Gly Ala Phe Ile Leu Leu Xaa Leu Met Gly
                               210
                                                  215
           205
Ile Val Leu Ile Cys Val Trp Trp Gln Asn Gly Xaa Xaa Ser Thr Xaa
Xaa
```

```
<210> 457
<211> 193
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -60..-1
```

<400> 457
Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu Pro
-60 -55 -50 -45

```
Cys Ser Gly Gln Gln Pro Phe Pro Phe Gly Ala Ser Asn Ile Pro
                                 - 35
              ~40
Leu Leu Cly Arg Ser Arg Lys Val Ala Arg Gly Ala Pro Val Leu
                             -20
Trp Pro Phe Leu Thr Trp Ile Asn Pro Ala Leu Ser Ile Cys Asp Pro
       -10
Leu Gly Ser Cys Gly Trp Xaa Cys His Thr Ala Gln Val Pro Ala Pro
               10
                                  15
Leu Gln Leu Pro Thr Ala Cys Pro Pro Leu Pro His Gly Thr Arg Ala
            25
                             30
Val Gly Pro Thr Pro Gly Leu Leu Pro Glu Ala Ala Ala Pro Xaa Thr
                       4.5
Xaa Gly Ala Leu Ser Ser Arg Ser Arg His Trp Ser Cys Ser Ile Val
                         60
                                           65
Xaa Cys Leu His Leu His Xaa Leu Leu Ser Val Glu Thr Arg Xaa Phe
                      75
Xaa Lys His Leu Leu Val Leu Val Ala Val Ala His Ser Val Leu
      . 90
                                    95
Glu Pro Pro Ala Leu Val Pro Asn Val Gln Cys Glu Met Cys Thr His
             105
                                110
Ser Gly Pro Arg Asp Leu Glu Ala Ala Val Val Ser Pro Ala Pro Trp
Glu
```

<210> 458 <211> 107 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -28..-1

<400> 458

Met Val Leu Thr Leu Gly Glu Ser Trp Pro Val Leu Val Gly Arg Arg -20 -15 Phe Leu Ser Leu Ser Ala Ala Asp Gly Ser Asp Gly Ser His Asp Ser -10 -5 1 Trp Asp Val Glu Arg Val Ala Glu Trp Pro Trp Leu Ser Gly Thr Ile 10 15 Arg Ala Val Ser His Thr Asp Val Thr Lys Lys Asp Leu Lys Val Cys 30 Val Glu Phe Xaa Gly Glu Ser Trp Arg Lys Arg Arg Trp Ile Glu Val 45 40 Tyr Ser Leu Leu Arg Lys Ala Phe Leu Val Lys His Asn Leu Val Leu - 60

Ala Glu Arg Lys Ser Pro Glu Ile Ser Trp Gly 70 75

<210> 459
<211> 121
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -13. -1

```
<400> 459
Met Leu Val Leu Arg Ser Ala Leu Thr Arg Ala Leu Ala Ser Arg Thr
           -10
Leu Ala Pro Gln Met Cys Ser Ser Phe Ala Thr Gly Pro Arg Gln Tyr
                       10
                                          15
Asp Gly Ile Phe Tyr Glu Phe Arg Ser Tyr Tyr Leu Lys Pro Ser Lys
20
                   25
                                     3.0
Met Asn Glu Phe Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr
                                   45
Ala His Ser Glu Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg
           55
                               60
Met Xaa Thr Val Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg
                           75
       70
Thr Glu Phe Gln Lys Ala Leu Ala Lys Asp Lys Glu Trp Gln Glu Gln
                   90
Phe Leu Ile Pro Asn Leu Ala Leu Asn
                   105
```

<210> 460 <211> 44 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -17..-1

<400> 460

 Met
 Lys
 Val
 Gly
 Val
 Leu
 Trp
 Leu
 Ile
 Ser
 Phe
 Phe
 Thr
 Phe
 Thr
 Asp

 Gly
 His
 Gly
 Gly
 Phe
 Leu
 Gly
 Val
 Ser
 Trp
 Cys
 Tyr
 Val
 Ser
 Tyr
 Leu

 1
 5
 5
 5
 5
 10
 15
 15

 Phe
 Ser
 Thr
 Ass
 Ser
 Pro
 Leu
 Ser
 Phe
 Arg
 Arg
 Ile

 20
 25
 25
 25
 25
 25
 25
 25

<210> 461 <211> 109 <212> PRT <213> Homo sapiens

<221> SIGNAL <222> -13..-1

<400> 461 Met Cys Leu Leu Thr Ala Leu Val Thr Gln Val Ile Ser Leu Arg Lys -10 Asn Ala Glu Arg Thr Cys Leu Cys Lys Arg Arg Trp Pro Trp Xaa Pro 15 Ser Pro Arg Ile Tyr Cys Ser Ser Thr Pro Cys Asp Ser Lys Phe Pro 25 30 Thr Val Tyr Ser Ser Ala Pro Phe His Ala Pro Leu Pro Val Gln Asn 45 40 Ser Leu Trp Gly His Pro Leu His Gly Cys Ser Trp Gln Cys His His 60 55 Pro Gln Gly Gln Asn Leu Gln Pro Ala Ser Leu Xaa Thr His Leu Ser Lys Pro Lys Arg His Phe Xaa Lys Lys Xaa Cys Gln Ala

85

90

95

```
<210> 462
<211> 143
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -41..-1
Met Ala Thr Ala Thr Glu Gln Trp Val Leu Val Glu Met Val Gln Ala
                        -35
Leu Tyr Glu Ala Pro Ala Tyr His Leu Ile Leu Glu Gly Ile Leu Ile
                   -20
Leu Trp Ile Ile Arg Leu Leu Phe Ser Lys Thr Tyr Lys Leu Gln Glu
               - 5
Arg Ser Asp Leu Thr Val Lys Glu Lys Glu Glu Leu Ile Glu Glu Trp
                           15
                                               20
Gln Pro Glu Pro Leu Val Pro Pro Val Pro Lys Asp His Pro Ala Leu
                      30
                                          35
Asn Tyr Asn Ile Val Ser Gly Pro Pro Ser His Lys Thr Val Val Asn
40
                   45
                                       50
Gly Lys Glu Cys Ile Asn Phe Ala Ser Phe Asn Phe Leu Gly Leu Leu
               60
Asp Asn Pro Arg Val Lys Ala Ala Ala Leu Ala Ser Leu Lys Lys Tyr
          75
                               80
Gly Val Gly Thr Cys Gly Pro Cys Gly Phe Tyr Gly Thr Phe Glu
```

<210> 463

<211> 232

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -30..-1

<400> 463

Met Ala Ala Thr Ser Gly Thr Asp Glu Pro Val Ser Gly Glu Leu Val -25 - 20 Ser Val Ala His Ala Leu Ser Leu Pro Ala Glu Ser Tyr Gly Asn Xaa -10 - 5 Xaa Asp Ile Glu Met Ala Trp Ala Met Arg Ala Met Gln His Ala Glu .10 15 Val Tyr Tyr Lys Leu Ile Ser Ser Val Asp Pro Gln Phe Leu Lys Leu 25 30 Thr Lys Val Asp Asp Gln Ile Tyr Ser Glu Phe Arg Lys Asn Phe Glu 40 45 Thr Leu Arg Ile Asp Val Leu Xaa Pro Glu Xaa Leu Lys Ser Glu Ser 60 Ala Lys Glu Pro Pro Gly Tyr Asn Ser Leu Pro Leu Lys Leu Leu Gly 75 Thr Gly Lys Ala Ile Thr Lys Leu Phe Ile Ser Val Phe Arg Thr Lys 90 Lys Glu Arg Lys Glu Ser Thr Met Glu Glu Lys Lys Glu Leu Thr Val

```
100
                      105
                                         110
Glu Lys Lys Arg Thr Pro Arg Met Glu Glu Arg Lys Glu Leu Ile Val
                120
                                     125
Glu Lys Lys Lys Arg Lys Glu Ser Thr Glu Lys Thr Lys Leu Thr Lys
              135
                                 140
Glu Glu Lys Lys Gly Lys Lys Leu Thr Lys Lys Ser Thr Lys Val Val
          150
                           155
                                                160
Lys Lys Leu Cys Lys Val Tyr Arg Glu Gln His Ser Arg Ser Tyr Asp
                          170
                                            175
Ser Ile Glu Thr Thr Ser Thr Thr Val Leu Leu Ala Gln Thr Pro Leu
                     185
  180
                                         190
Val Lys Cys Lys Phe Leu Tyr Asn
                   200
```

<210> 464 <211> 61 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -21..-1

<210> 465
<211> 34
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19...1

<210> 466 <211> 215 <212> PRT <213> Homo sapiens

<220>

```
<221> SIGNAL
<222> -54..-1
<400> 466
Met Asn Xaa Tyr Ala Ser Pro Phe Asn Xaa Gln Leu Xaa Tyr Leu Xaa
           -50
                       -45
Leu Ser Arg Phe Glu Cys Val His Arg Asp Gly Arg Val Ile Thr Leu
Ser Tyr Gln Glu Gln Glu Leu Gln Asp Phe Leu Leu Ser Gln Met Ser
     -20 -15
Gln His Gln Val His Ala Val Gln Gln Leu Ala Lys Val Met Gly Trp
                     1
Gln Val Leu Ser Phe Ser Asn His Val Gly Leu Gly Pro Ile Glu Ser
                                 20
Xaa Gly Asn Ala Ser Ala Ile Thr Val Ala Pro Gln Val Val Thr Met
                           35
        30
Leu Phe Gln Phe Val Met Asp Leu Lys Val Ala Ala Arg Leu Trp Phe
                          50
Ser Phe Leu Val Thr Asn Val Lys Thr Phe Gln Lys Val Met Phe Tyr
Lys Ile Thr Asn Gly Val Ile Phe Val Gly His Ser Lys Lys Phe Ser
                  80
                                    85
Gly Ile Lys Trp Lys Val Xaa Ile Leu Phe Ile Lys Trp Xaa Cys Leu
              95
                                 100
                                                   105
Cys Leu His Leu Ala Leu Val Tyr Tyr Asp Phe Phe Gln Met Phe Pro
           110
                              115
                                                120
Lys Xaa Val Ser Xaa Asn Phe Asp Leu Lys Cys Leu Gln Ile Asn Tyr
      125
                        130
                                       135
Lys His Lys Glu Glu Ile Thr Ser Lys Arg Val Leu Phe Leu Lys Ile
                     145
Ile Ile Arg Lys Cys Phe Ile
```

<210> 468
<211> 85
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24...1
<400> 468

```
Met Cys Ser His Ala Ser Met Ser Phe His Thr Leu Phe His Leu Leu
                                   -15
               -20
Phe Leu Pro His Tyr Ile Glu Thr Phe Lys Pro Gln Ser Lys His Cys
                             1
         - 5
Phe Phe Trp Ile Ala Ala Phe Leu Thr Ser Leu Leu Thr Pro Gln Ser
                       15
                                          20
Leu Gln Gly Phe His Ser Ser Leu Cys Ala Leu Arg Ser Gln His Phe
                   30
                                       3.5
Pro Ser Thr Cys Asn Cys Phe Cys Tyr Leu Thr Ile Ile Ala Leu Xaa
               45
                                   50
Tyr Trp Asp Asn Leu
            60
```

<210> 469
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -16..-1

<400> 469
Met Leu Arg Ile Ala Leu Thr Leu Ile Pro Ser Met Leu

Met Leu Arg Ile Ala Leu Thr Leu Ile Pro Ser Met Leu Ser Arg Ala
-15
-10
-10
-5
Ala Gly Trp Cys Trp Tyr Lys Glu Pro Thr Gln Gln Phe Ser Tyr Leu
1 5 10
15
Cys Leu Pro Cys Leu Ser Trp Asn-Lys Lys Gly Asn Val Leu Gln Leu
20
25
25
26
27
28
28
29
20
30

<210> 470 <211> 67 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<222> -43..-1

<210> 471 <211> 63 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -15..-1
<400> 471
Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe Ala Arg Ala Leu
       -10
                     - 5
Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser Glu Lys His Arg
                           10
Leu Glu Lys Cys Arg Glu Leu Glu Ser Ser His Ser Ala Pro Gly Ser
    20
                25
                                30
Thr Gln His Arg Arg Lys Thr Thr Arg Arg Asn Tyr Ser Ser Ala
                 40
<210> 472
<211> 179
<212> PRT
<213> Homo sapiens
```

<220> <221> SIGNAL <222> -58..-1 <400> 472 Met Ser Thr Gly Gln Leu Tyr Arg Met Glu Asp Ile Gly Arg Phe His -55 -50 -45 Ser Gln Gln Pro Gly Ser Leu Thr Pro Ser Ser Pro Thr Val Gly Glu -35 Ile Ile Tyr Asn Asn Thr Arg Asn Thr Leu Gly Trp Ile Gly Gly Ile -25 -20 -15 Leu Met Gly Ser Phe Gln Gly Thr Ile Ala Gly Gln Gly Thr Gly Ala -10 -5 1 Thr Ser Ile Ser Glu Leu Cys Lys Gly Gln Glu Leu Glu Pro Ser Gly 15 10 Ala Gly Leu Thr Val Ala Pro Pro Gln Ala Val Ser Leu Gln Gly Ile 30 Tyr Thr Leu Pro Trp Leu Leu Gln Leu Phe His Ser Thr Ala Leu Xaa 45 50 Xaa Xaa Gln Gln Pro Asn Gly Ser Leu Ser Leu Asn Ile Ser Ser Ser 60 65 His Ala Pro Xaa Pro Xaa Thr Cys Thr Leu Glu Pro Gly Val Asp Pro 75 80 Thr Arg Xaa Val Cys Ile Asn Pro His Pro Pro Pro Pro Ile Leu Lys 95 . 100 Xaa Pro Leu Ser Pro Tyr Pro Lys Pro Gln Leu Gly Thr His Ala Gly 115 105 110 Gln Val Asn

```
<210> 473
<211> 238
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -71..-1
```

120

```
<400> 473
Met Xaa Xaa Phe Thr Asp Pro Ser Ser Val Asn Glu Lys Lys Arg Arg
                        -65
                                            -60
Glu Arg Glu Glu Arg Gln Asn Ile Val Leu Trp Arg Gln Pro Leu Ile
                    - 50
                                        -45
Thr Leu Gln Tyr Phe Ser Leu Glu Ile Leu Val Ile Leu Lys Glu Trp
                                    - 30
Thr Ser Lys Leu Trp His Arg Gln Ser Ile Val Val Ser Phe Leu Leu
Leu Leu Ala Gly Leu Ile Ala Thr Tyr Tyr Val Glu Gly Val His Gln
Gln Tyr Val Gln Arg Ile Glu Lys Gln Phe Leu Leu Tyr Ala Tyr Trp
                                        20
Ile Gly Leu Gly Ile Leu Ser Ser Val Gly Leu Gly Thr Gly Leu His
                30
Thr Phe Leu Leu Tyr Leu Gly Pro His Ile Ala Ser Val Thr Leu Ala
            45
                                50
Ala Tyr Glu Cys Asn Ser Val Asn Phe Pro Glu Pro Pro Tyr Pro Asp
                            65
Gln Ile Ile Cys Pro Asp Glu Glu Gly Thr Glu Gly Thr Ile Ser Leu
                        80
Trp Ser Ile Ile Ser Lys Val Arg Ile Glu Ala Cys Met Trp Gly Ile
                    95
                                        100
Gly Thr Ala Ile Gly Glu Leu Pro Pro Tyr Phe Met Ala Arg Ala Ala
                                    115
Arg Leu Ser Gly Ala Glu Pro Asp Asp Glu Glu Tyr Gln Glu Phe Glu
           125
                               130
Glu Met Leu Glu His Ala Glu Ser Ala Gln Val Arg Thr Val Gly Ile
                           145
                                                150
Glu Asn Arg Thr Leu Tyr Phe Phe Leu Lys Arg Leu Leu Arg
                        160
```

<210> 474 <211> 178 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -37..-1

<400> 474 Met Glu Arg Gln Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe -35 -30 -25 Gln His Gln Gly Ala Val Glu Leu Leu Val Phe Asn Phe Leu Leu Ile -15 Leu Thr Ile Leu Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr Gly Gly Ala Met Val Tyr Gly Leu Xaa Met Gly Leu 20 Ile Leu Xaa Tyr Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Xaa Val 35 Tyr Asp Cys Val Lys Leu Thr Phe Ser Pro Ser Thr Leu Leu Val Asn 50 Ile Thr Asp Gln Val Tyr Glu Tyr Lys Tyr Lys Arg Glu Ile Ser Gln 70 65 His Xaa Ile Asn Pro His Xaa Gly Asn Ala Ile Leu Glu Lys Met Thr 85 Phe Asp Pro Xaa Ile Phe Phe Asn Val Leu Leu Pro Pro Ile Ile Phe

```
95
                           100
His Ala Gly Tyr Ser Leu Lys Lys Arg His Phe Phe Gln Asn Leu Gly
             115
                               120
Ser Ile Leu Thr Tyr Ala Phe Leu Gly Thr Ala Ile Ser Cys Ile Val
          , 130
Ile Gly
140
<210> 475
<211> 96
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 475
Met Ser Met Gln Phe Leu Phe Lys Met Val Ala Leu Cys Cys Cys Leu
                -15
                                     -10
Trp Lys Ile Ser Gly Cys Glu Glu Val Pro Leu Thr Tyr Asn Leu Leu
              1
                     5
Lys Cys Leu Leu Asp Lys Ala His Cys Val Leu Leu Thr Pro Cys Gly
       15
                   20
Tyr Ile Phe Ser Leu Ile Ser Pro Glu Ile Leu Lys Leu Thr Leu Ile
   30
                     35
Thr Leu Xaa Ile Leu Leu Ile Leu Lys Asn Leu His Leu Leu Trp Leu
 45 50
                             55
Thr Val Ser Ser Xaa Cys Val His Arg Ser Ser Ala Arg Lys Glu Lys
                65
<210> 476
<211> 41
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
<400> 476
Met His Thr Phe Ala Asn Asp Arg Gly Leu Tyr Arg Ile Leu Leu Leu
          -20 -15
His Phe Tyr Cys Leu Leu Arg Ser Ser Glu Tyr Ile Leu Gly Tyr Lys
        - 5
                 1
Val Leu Gly Val Phe Phe Pro Ile Leu
   10
<210> 477
<211> 113
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1
```

```
<400> 477
Met Arg Xaa Lys Trp Lys Met Gly Gly Met Lys Tyr Ile Phe Ser Leu
                           -20
Leu Phe Phe Leu Leu Glu Gly Gly Xaa Thr Glu Gln Val Xaa His
                       - 5
Ser Glu Thr Tyr Cys Met Phe Gln Asp Lys Lys Tyr Arg Val Gly Glu
                                  15
              10
Arg Trp His Pro Tyr Leu Glu Pro Tyr Gly Leu Val Tyr Cys Val Asn
           25
                               30
Cys Ile Cys Ser Glu Asn Gly Asn Val Leu Cys Ser Arg Val Arg Cys
                           45
Pro Asn Val His Cys Leu Ser Pro Val His Ile Pro His Leu Cys Cys
                     60
Pro Arg Cys Pro Glu Asp Ser Leu Pro Pro Val Asn Asn Xaa Val Thr
```

```
<210> 478
<211> 250
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
```

<222> -18..-1

<400> 478 Met Arg Ile Leu Gln Leu Ile Leu Leu Ala Leu Ala Thr Gly Leu Val -15 -10 Gly Gly Glu Thr Arg Ile Ile Lys Gly Phe Glu Cys Lys Pro His Ser Gln Pro Trp Gln Ala Ala Leu Phe Glu Lys Thr Arg Leu Leu Cys Gly 20 25 Ala Thr Leu Ile Ala Pro Arg Trp Leu Leu Thr Ala Ala His Cys Leu Lys Pro Arg Tyr Ile Xaa His Leu Gly Gln His Asn Leu Gln Lys Glu 50 55 Glu Gly Cys Glu Gln Thr Arg Thr Ala Thr Glu Ser Phe Pro His Pro 70 Gly Phe Asn Asn Ser Leu Pro Asn Lys Asp Xaa Xaa Asn Asp Ile Met 85 Leu Val Xaa Met Xaa Ser Pro Val Ser Ile Thr Trp Ala Val Arg Pro 100 105 Leu Thr Leu Ser Ser Arg Cys Val Thr Ala Gly Thr Ser Cys Leu Ile 115 120 Ser Gly Trp Gly Ser Thr Ser Ser Pro Gln Leu Arg Leu Pro His Thr 135 130 Leu Arg Cys Ala Asn Ile Thr Ile Ile Glu His Gln Lys Cys Glu Asn 150 Ala Tyr Pro Gly Asn Ile Thr Asp Thr Met Val Cys Ala Ser Val Gln 165 170 Glu Gly Gly Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val 180 185 Cys Asn Gln Ser Leu Gln Gly Ile Ile Ser Trp Gly Gln Asp Pro Cys 200 195 Ala Ile Thr Arg Lys Pro Gly Val Tyr Thr Lys Val Cys Lys Tyr Val 215 210 Asp Trp Ile Gln Glu Thr Met Lys Asn Asn

```
<210> 479
<211> 151
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 479
Met Ala Ala Ser Thr Ser Met Val Pro Val Ala Val Thr Ala Ala Val
                    -15
Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu Arg Glu Ile
Lys Lys Gln Leu Leu Leu Ile Ala Gly Leu Thr Arg Glu Arg Gly Leu
                               20
Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser Leu Pro Ala
 3.0
                          35
Leu Pro Leu Ala Glu Leu Gln Pro Pro Pro Pro Ile Thr Glu Glu Asp
                       50
                                       55
Ala Gln Asp Met Asp Ala Tyr Thr Leu Ala Lys Ala Tyr Phe Asp Val
                  65
                                      70
Lys Glu Tyr Asp Arg Ala Ala His Phe Leu His Gly Cys Asn Ala Arg
               80
                                85
Lys Ala Tyr Phe Leu Tyr Met Tyr Ser Arg Tyr Leu Val Arg Ala Ile
                               100
Leu Lys Cys His Ser Ala Phe Ser Glu Thr Ser Ile Phe Arg Thr Asn
      110
                          115
Gly Lys Val Lys Ser Phe Lys
   125
                       130
<210> 480
<211> 239
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 480
Met Pro Arg Lys Arg Lys Cys Asp Leu Arg Ala Val Arg Val Gly Leu
                  -20
                               -15
Leu Leu Gly Gly Gly Val Tyr Gly Ser Arg Phe Arg Phe Thr Phe
                                   1
Pro Gly Cys Arg Ala Leu Ser Pro Trp Arg Val Arg Xaa Gln Arg Arg
       10
                          15
Arg Cys Glu Met Ser Thr Met Phe Ala Asp Thr Leu Leu Ile Val Phe
                       30
Ile Ser Val Cys Thr Ala Leu Leu Ala Glu Gly Ile Thr Trp Val Leu
                   45
                                      50
Val Tyr Arg Thr Asp Lys Tyr Lys Arg Leu Lys Ala Glu Val Glu Lys
                                 65
Gln Ser Lys Lys Leu Glu Lys Lys Lys Glu Thr Ile Thr Glu Ser Ala
           75
                               80
                                                  85
```

Gly Arg Gln Gln Lýs Lys Lys Ile Glu Arg Xaa Xaa Xaa Leu Xaa 90 95 100

```
Asn Asn Arg Asp Leu Ser Met Val Arg Met Lys Ser Met Phe Ala
                   . 110
                                           115
Ile Gly Phe Cys Phe Thr Ala Leu Met Gly Met Phe Asn Ser Ile Phe
                   125
                                      130
Asp Gly Arg Val Val Ala Lys Leu Pro Phe Thr Pro Leu Ser Xaa Xaa
               140
                                  145
Xaa Gly Leu Ser His Arg Asn Leu Leu Gly Asp Asp Thr Thr Asp Cys
           155
                              160
                                                 165
Ser Phe Ile Phe Leu Xaa Ile Leu Cys Thr Met Ser Ile Arg Gln Asn
                         . 175
                                              180
Ile Gln Lys Ile Leu Gly Leu Ala Pro Ser Arg Ala Ala Thr Lys Gln
                       190
                                           195
Ala Gly Gly Phe Leu Gly Pro Pro Pro Pro Ser Gly Lys Phe Ser
                   205
```

```
<210> 481
<211> 208
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -92..-1
```

## <400> 481

Met Arg Glu Pro Gln Lys Arg Thr Ala Thr Ile Ala Lys Xaa Xaa Ala - 90 -85 -80 Xaa Glu Gly Leu Arg Asp Pro Tyr Gly Arg Leu Cys Gly Ser Glu His -70 -65 Pro Arg Arg Pro Pro Glu Arg Pro Glu Glu Asp Pro Ser Thr Pro Glu -50 -55 Glu Ala Ser Thr Thr Pro Glu Glu Ala Ser Ser Thr Ala Gln Ala Gln - 35 -40 Lys Pro Ser Val Pro Arg Ser Asn Phe Gln Gly Thr Lys Lys Ser Leu -20 -25 Leu Met Ser Ile Leu Ala Leu Ile Phe Ile Met Gly Asn Ser Ala Lys Glu Ala Leu Val Trp Lys Val Leu Gly Lys Leu Gly Met Gln Pro Gly 10 Arg Xaa His Ser Ile Phe Gly Asp Pro Lys Lys Ile Val Thr Glu Xaa 30 25 Phe Val Arg Arg Gly Tyr Leu Ile Tyr Xaa Pro Val Pro Arg Xaa Ser 40 Pro Val Glu Tyr Xaa Phe Phe Trp Gly Pro Arg Ala His Val Glu Ser 60 Ser Xaa Leu Lys Xaa Xaa His Phe Val Ala Arg Val Arg Asn Arg Cys 75 Ser Lys Asp Trp Pro Cys Asn Tyr Asp Trp Asp Ser Asp Asp Ala 90 95 Glu Val Glu Ala Ile Leu Asn Ser Gly Ala Xaa Gly Tyr Ser Ala Pro

```
<210> 482
<211> 86
<212> PRT
```

<213> Homo sapiens

<220>

Ĭ.

```
<221> SIGNAL
<222> -39..-1
<400> 482
Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg Val
          -35 -30 -25
Met Asn Ser Arg Gly Ile Trp Leu Ser Tyr Val Leu Ala Ile Gly Leu
          -20
                        -15
                                  -10
Leu His Ile Val Leu Leu Ser Ile Pro Phe Val Ser Val Pro Val Val
 -5
                    1
Trp Thr Leu Thr Asn Leu Ile His Asn Met Gly Met Tyr Ile Phe Leu
    15 20
His Thr Val Lys Gly Thr Pro Phe Glu Thr Pro Asp Gln Gly Lys Ala
           30
Arg Leu Leu Thr His Trp
         45
<210> 483
<211> 40
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1
<400> 483
Met Arg Thr Leu Phe Gly Ala Val Arg Ala Pro Phe Ser Ser Leu Thr
-25 -20 -15
Leu Leu Leu Ile Thr Pro Ser Pro Ser Pro Leu Leu Phe Asp Arg Gly
 -10 -5
                               1
Leu Ser Leu Arg Ser Ala Met Ser
            10
<210> 484
<211> 65
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 484
Met Leu Gly Phe Phe Leu Phe Leu Ser Phe Val Leu Met Tyr Asp Gly
        -10 -5
Leu Arg Leu Phe Gly Ile Leu Ser Thr Cys Arg Val His His Thr Met
                           10
Asn Gln Phe Leu Ile Asp Ile Ser Ser Phe Thr Ser Arg Val Lys Lys
                       25
  20
Lys Ile Phe Leu Phe Tyr Ala Phe Xaa Gly Cys Xaa Phe Gln Ser Ala
```

<210> 485 <211> 130

```
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -55..-1
<400> 485
Met Ala Met Trp Asn Arg Pro Xaa Xaa Xaa Leu Pro Gln Gln Pro Leu
                                        -45
                   -50
Xaa Ala Glu Pro Thr Ala Glu Gly Glu Pro His Leu Pro Thr Gly Arg
                - 35
                                     -30
Xaa Xaa Thr Glu Ala Asn Arg Phe Ala Tyr Ala Ala Leu Cys Gly Ile
                                - 15
            -20
Ser Leu Ser Gln Leu Phe Pro Glu Pro Glu His Ser Ser Phe Cys Thr
                           1.
Glu Phe Met Ala Gly Leu Val Xaa Trp Leu Glu Leu Ser Glu Ala Val
                   15
                                        20
Leu Pro Thr Met Thr Ala Phe Ala Ser Gly Leu Gly Gly Glu Gly Xaa
                                   35
Xaa Cys Val Cys Ser Asn Phe Thr Glu Gly Pro His Leu Glu Gly Arg
                                50
          45
Pro Asp Gly Asp His Ser Gly Pro Ser Glu Leu Leu Thr Gln Gly Trp
                            65
Ala Leu
    75
<210> 486
                               - et .
<211> 209
 <212> PRT
<213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -84..-1
<400> 486
Met Val Asn Phe Pro Gln Lys Ile Ala Gly Glu Leu Tyr Gly Pro Leu
                                     -75
Met Leu Val Phe Thr Leu Val Ala Ile Leu Leu His Gly Met Lys Thr
                                -60
 Ser Asp Thr Ile Ile Arg Glu Gly Thr Leu Met Gly Thr Ala Ile Gly
                                                 -40
                             -45
 Thr Cys Phe Gly Tyr Trp Leu Gly Val Ser Ser Phe Ile Tyr Phe Leu
                         -30
                                             -25
 Ala Tyr Leu Cys Asn Ala Gln Ile Thr Met Leu Gln Met Leu Ala Leu
                                         -10
                     -15
 Leu Gly Tyr Gly Leu Phe Gly His Cys Ile Val Leu Phe Ile Thr Tyr
```

Leu Gly Tyr Gly Leu Phe Gly His Cys Ile Val Leu Phe Ile Thr Tyr 1 5 10

Asn Ile His Leu Arg Ala Leu Phe Tyr Leu Phe Trp Leu Leu Val Gly 15 20 25

Gly Leu Ser Thr Leu Arg Met Val Ala Val Leu Val Ser Arg Thr Val 30 35 40

Gly Pro Thr Xaa Arg Xaa Leu Leu Cys Gly Thr Leu Ala Ala Leu His 50 60

Met Leu Phe Leu Leu Tyr Leu His Phe Ala Tyr His Lys Xaa Val Xaa 65 70 75

Gly Ile Leu Asp Thr Leu Glu Gly Pro Asn Ile Pro Pro Ile Gln Arg 80 85 90

Val Pro Arg Asp Ile Pro Ala Met Leu Pro Ala Ala Arg Leu Pro Thr

```
100
                                           105
Thr Val Leu Asn Ala Thr Ala Lys Ala Val Ala Val Thr Leu Gln Ser
              115
                                120
His
125
<210> 487
<211> 36
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1
<400> 487
Met Gly Trp Gln Arg Trp Trp Cys Phe His Leu Gln Ala Glu Ala Ser
                -10
Ala His Pro Pro Gln Gly Leu Gln Ala Gln Phe Ser Cys Cys Pro Trp
 1
           5
                                10
Val Gly Ile Cys
<210> 488
<211> 44
<212> PRT
<213> Homo sapiens
  7.1
<220>
<221> SIGNAL
<222> -29. ::=1
<400> 488
Met Met Ser Ser Glu Leu Arg Arg Asn Pro His Phe Leu Lys Ser Asn
        -25
                            -20
                                        -15
Leu Phe Leu Gln Leu Leu Val Ser His Glu Ile Val Cys Ala Thr Glu
   -10
                          - 5
Thr Val Thr Thr Asn Phe Leu Arg His Glu Lys Ala
<210> 489
<211> 163
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -52..-1
<400> 489
Met Glu His Tyr Arg Lys Ala Gly Ser Val Glu Leu Pro Ala Pro Ser
 -50
                         -45
                                           - 40
Pro Met Pro Gln Leu Pro Pro Asp Thr Leu Glu Met Arg Val Arg Asp
                    -30
                                      - 25
Gly Ser Lys Ile Arg Asn Leu Leu Gly Leu Ala Leu Gly Arg Leu Glu
                                    - 10
                 -15
Gly Gly Ser Ala Arg His Val Val Phe Ser Gly Ser Gly Arg Ala Ala
```

Gly Lys Ala Val Ser Cys Ala Glu Ile Val Lys Arg Arg Val Pro Gly 20 Leu His Gln Leu Thr Lys Leu Xaa Phe Leu Gln Thr Glu Asp Ser Trp 35 Val Pro Xaa Ser Pro Asp Thr Gly Leu Xaa Pro Leu Thr Val Arg Arg 50 55 His Val Pro Ala Xaa Trp Val Leu Leu Xaa Arg Asp Pro Leu Asp Pro 65 70 Asn Glu Cys Gly Tyr Gln Pro Pro Gly Ala Pro Pro Gly Leu Gly Ser 85 . 80 Met Pro Ser Ser Cys Gly Pro Arg Ser Xaa Lys Arg Ala Xaa Xaa 100 105 Thr Arg Ser 110

<210> 490 <211> 64 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -47..-1

<210> 491 <211> 218 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -50..-1

Met His His Gly Leu Thr Pro Leu Leu Cly Val His Glu Gln Lys -40 -50 -45 Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala -25 -30 Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly -5 -10 -15 Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Lys Lys Tyr Ala Val Ser Ser 25 Arg His Asn Val Ile Cys Gln Leu Leu Ser Asp Tyr Lys Xaa Lys Gln 40 Xaa Leu Lys Val Ser Ser Glu Asn Ser Asn Pro Xaa Gln Asp Leu Lys

```
50
Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Lys Gly Ser Glu Asn Ser
 65
                               75
               70
Gln Pro Glu Glu Met Ser Gln Glu Pro Glu Ile Asn Xaa Gly Gly Asp
                   85
Arg Lys Val Glu Xaa Xaa Met Lys Lys His Gly Ser Xaa His Met Gly
95
                100
                                105
Phe Pro Xaa Asn Leu Xaa Asn Gly Ala Thr Ala Asp Asn Gly Asp Asp
           115
                            120 125
Gly Leu Ile Pro Pro Xaa Lys Xaa Xaa Thr Pro Glu Ser Xaa Gln Phe
                         135
Pro Asp Thr Glu Asn Glu Gln Tyr His Arg Asp Phe Ser Gly His Pro
          150
Xaa Phe Pro Thr Thr Leu Pro Ile Lys Gln
  160 165
```

```
<210> 492
<211> 216
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
```

<400> 492 Met Val Cys Val Leu Val Leu Ala Ala Ala Ala Gly Ala Val Ala Val -10 -15 - 5 Phe Leu Ile Leu Arg Ile Trp Val Val Leu Arg Ser Met Asp Val Thr 10 Pro Arg Glu Ser Leu Ser Ile Leu Val Val Ala Gly Ser Gly Gly His 25 Thr Thr Glu Ile Leu Arg Leu Leu Gly Ser Leu Ser Asn Ala Tyr Ser 40 45 Pro Arg His Tyr Val Ile Ala Asp Thr Asp Glu Met Ser Ala Asn Lys 60 55 Ile Asn Ser Phe Glu Leu Xaa Arg Xaa Asp Arg Xaa Pro Ser Asn Met Xaa Thr Lys Tyr Tyr Ile His Arg Ile Pro Xaa Ser Arg Glu Val Gln 90 Gln Ser Trp Pro Ser Thr Val Xaa Thr Thr Leu His Ser Met Trp Leu 105 100 110 Ser Xaa Pro Leu Ile His Arg Val Lys Pro Xaa Leu Val Leu Cys Asn 120 125 Gly Pro Gly Thr Cys Val Pro Ile Cys Val Ser Ala Leu Leu Leu Gly 135 140 Ile Leu Gly Ile Lys Lys Val Ile Ile Val Tyr Val Glu Ser Ile Cys 150 155 Arg Val Lys Thr Leu Ser Met Ser Gly Lys Ile Leu Phe His Leu Ser 170 165 Asn Tyr Phe Ile Val Gln Trp Pro Ala Leu Lys Glu Lys Tyr Pro Lys 185 Ser Val Tyr Leu Gly Arg Ile Val

<210> 493
<211> 134
<212> PRT

```
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 493
Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala Gly
                -15
Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg Thr
Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Xaa His Pro Glu Ala
                        20
Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu Ile
                  35
Asp Arg Glu Asn Phe Val Asp Ile Val Xaa Ala Lys Leu Lys Ile Pro
                                    55
Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser Arg
Gly Gly Pro Phe Gln Arg Trp His Leu Asp Glu Val Phe Leu Glu Leu
                            85
Lys Asp Gly Gln Gln Ile Pro Val Phe Lys Leu Ser Gly Glu Asn Gly
                        100
Asp Glu Val Lys Lys Glu
<210> 494
<211> 85
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 494
Met Ala Val Thr Ala Leu Ala Ala Xaa Thr Trp Leu Gly Val Trp Gly
                        -10
Val Arg Thr Met Gln Ala Arg Gly Phe Gly Ser Asp Gln Ser Glu Asn
Val Asp Arg Gly Ala Gly Ser Ile Arg Glu Ala Gly Gly Ala Phe Gly
Lys Arg Glu Gln Ala Glu Glu Glu Arg Tyr Phe Arg Ala Gln Ser Thr
Glu Gln Leu Ala Xaa Leu Lys Lys Xaa His Glu Glu Glu Ile Val His
His Arg Glu Gly Asp
<210> 495
```

<210> 495
<211> 292
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -29..-1

<400> 495 Met His Gly Leu Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe -25 -20 Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr - 10 - 5 Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr 10 15 Leu Leu Pro Tyr Leu Leu Leu Gly Val Asn Leu Phe Phe Thr 30 Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu 40 4.5 Leu Phe Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe Pro Lys Asn 60 Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Xaa His Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His His Cys Val 90 Trp Val Asn Asn Cys Ile Gly Ala Trp Asn Ile Arg Xaa Phe Leu Ile 105 110 Tyr Val Leu Thr Leu Thr Ala Ser Ala Ala Thr Val Ala Ile Val Ser 125 ~ 130 120 Thr Thr Phe Leu Val His Leu Val Val Met Ser Asp Leu Tyr Gln Glu 140 145 Thr Tyr Ile Asp Asp Leu Gly His Leu His Val Met Asp Thr Val Phe 160 155 Leu Ile Gln Tyr Leu Phe Leu Thr Phe Pro Arg Ile Val Phe Met Leu 170 175 Gly Phe Val Val Leu Xaa Phe Leu Leu Gly Gly Tyr Leu Leu Phe 185 190 Val Leu Tyr Leu Ala Ala Thr Asn Gln Thr Thr Asn Glu Trp Tyr Arg 200 205 Xaa Asp Trp Ala Trp Cys Gln Arg Cys Pro Leu Val Ala Trp Pro Pro 215 220 Ser Ala Glu Pro Gln Val His Arg Asn Ile His Ser His Gly Leu Arg 235 240 Xaa Asn Leu Gln Glu Ile Phe Leu Pro Ala Phe Pro Cys His Glu Arg 250 Lys Lys Gln Glu 260

<210> 496 <211> 122 <212> PRT <213> Homo sapiens

<221> SIGNAL <222> -56..-1

<400> 496
Met Thr Gly Phe Leu Leu Pro Pro Ala Ser Arg Gly Thr Arg Arg Ser
 -55
 -50
 -45
Cys Ser Arg Ser Arg Lys Arg Gln Thr Arg Arg Arg Arg Arg Arg Pro Ser
 -40
 -35
 -30
 -25
Ser Phe Val Ala Ser Cys Pro Thr Leu Leu Pro Phe Ala Cys Val Pro
 -20
 -15
 -10
Gly Ala Ser Pro Thr Thr Leu Ala Phe Pro Pro Val Xaa Leu Thr Gly
 -5
 1
 5
Pro Xaa Thr Asp Gly Ile Pro Phe Ala Leu Xaa Ser Ala Ala Gly Pro
 10

```
Phe Cys Ala Ser Phe Pro Ser Gly Xaa Leu Ser Pro Pro Gly Pro Leu 25 30 35 40

Pro Gly Val Arg Gly Leu Pro Leu Pro Ser Val Phe Tyr Ser Cys Gly 45 50 55

Ala His Pro Lys Val Leu Lys Val Ala Leu 60 65
```

<210> 497 <211> 59 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -28...1

<400> 497

 Met
 Leu
 Xaa
 Leu
 Ser
 Arg
 Ala
 Thr
 Lys
 Xaa
 Gly
 Arg
 Ala
 Arg
 Trp
 Leu

 Met
 Pro
 Val
 Ile
 Pro
 Ala
 Leu
 Glu
 Ala
 Ala
 Ala
 Gly
 Gly
 Gly
 Ser
 Arg

 Gly
 Gln
 Glu
 Phe
 Glu
 Thr
 Ser
 Leu
 Ala
 Asn
 Met
 Glu
 Thr
 Glu
 Ala
 Gly

 5
 10
 10
 15
 20

 Glu
 Leu
 Leu
 Leu
 Arg
 Arg
 Arg
 Leu
 Gln

 30
 25
 30
 30
 30
 30
 30

<210> 498 <211> 99 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -13..-1

<400> 498

 Met
 His
 Leu
 Leu
 Ser
 Asn
 Trp
 Ala
 Asn
 Pro
 Ala
 Ser
 Ser
 Arg
 Arg
 Pro

 Ser
 Met
 Ala
 Ala
 Ser
 Gly
 Thr
 Ser
 Trp
 Ile
 Ser
 Ser
 Thr
 Leu
 Ala
 His
 His
 His
 His
 His
 Ser
 Gly
 Arg
 Arg
 Ile
 Ser
 Ser
 Thr
 Leu
 Ala
 His
 Arg
 Ile
 Arg
 Ile
 Ile

<210> 499 <211> 99 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -13..-1
<400> 499
Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg Arg Pro
         -10
                            - 5
Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu Ala His
                       10
                                          15
Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys Trp Arg
                   25
                                       30
Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn Ser Ser
                          45
              40
Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr Pro Met
                              60
Arg Arg Ser Ser Cys His Leu Xaa Cys Gln Val Ile Phe Leu Leu Gly
                           75
Arg Gln Leu
   85
<210> 500
<211> 108
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 500
Met Ser Leu Thr Ser Ser Ser Ser Val Arg Val Glu Trp Ile Ala Ala
                   -20
                                       -15
Val Thr Ile Ala Ala Gly Thr Ala Ala Ile Gly Tyr Leu Ala Tyr Lys
               -5
Arg Phe Tyr Val Lys Asp His Arg Asn Lys Ala Met Ile Asn Leu His
      10
                           15
Ile Gln Lys Asp Asn Pro Lys Ile Val His Ala Phe Asp Met Glu Asp
                                          35
                      30
Leu Gly Asp Lys Ala Val Tyr Cys Arg Cys Trp Arg Ser Lys Lys Phe
                                       50
                   45
Pro Phe Cys Asp Gly Ala His Thr Lys His Asn Glu Glu Thr Gly Asp
               60
Asn Val Gly Pro Leu Ile Ile Lys Lys Lys Glu Thr
            75
                               80
<210> 501
<211> 183
<212> PRT
<213> Homo sapiens
<221> SIGNAL
<222> -15..-1
<400> 501
```

Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu Ala Val Leu Ala Trp
-15 -10 -5 1
Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg Met Lys Ser Arg Glu

```
10
Gln Gly Arg Arg Leu Gly Ala Glu Ser Arg Thr Leu Leu Val Ile Ala
                           25
His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro Thr Val Leu Gly Leu
                       40
                                           45
Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys Phe Ser Ala Gly Asn
                    55
                                      60
Tyr Tyr Asn Gln Gly Glu Thr Arg Lys Lys Glu Leu Leu Gln Ser Cys
                                   75
Asp Val Leu Gly Ile Pro Leu Ser Ser Val Met Ile Ile Asp Asn Arg
           85
                                90
Asp Phe Pro Xaa Asp Pro Gly Met Gln Trp Asp Thr Xaa His Val Ala
                           105
                                              . 110
Xaa Val Leu Leu Gln His Ile Glu Val Asn Gly Ile Asn Leu Val Val
                       120
                                          125
Thr Phe Asp Ala Gly Gly Xaa Ser Gly His Ser Asn His Ile Ala Leu
                   135
                                       140
Tyr Ala Ala Val Arg Lys Leu Glu Gly Gln Ile Cys Lys Pro Cys Gly
               150
                                   155
Thr Gly Gln Asp Phe Lys Glu
            165
```

```
<210> 502
<211> 98
```

<212> PRT

<213 > Homo sapiens

<220>

<221> SIGNAL

<222> -15..-1

<400> 502

Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu Ala Val Leu Ala Trp
-15 -10 -5

Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg Met Lys Ser Arg Glu
5

Gln Gly Xaa Arg Leu Gly Ala Glu Ser Arg Thr Leu Leu Val Ile Ala
20

His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro Thr Val Leu Gly Leu
35

Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys Phe Ser Ala Val Phe
50

Arg Arg Glu Leu Ser Glu Tyr Thr Glu Xaa Leu Thr Ser Glu Pro Leu
70

ورا مرجي

Xaa Ala

<210> 503 <211> 183

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -57..-1

<400> 503

Met Asp Val Thr Gly Asp Glu Glu Glu Ile Lys Gln Glu Ile Asn
-55 -50 -45

Met Leu Lys Lys Tyr Ser His His Arg Asn Ile Ala Thr Tyr Tyr Gly -35 Ala Phe Ile Lys Lys Asn Pro Pro Gly Met Asp Asp Gln Leu Trp Leu -15 Val Met Glu Phe Cys Gly Ala Gly Ser Val Thr Asp Leu Ile Lys Asn Thr Lys Gly Asn Thr Leu Lys Glu Glu Trp Ile Ala Tyr Ile Cys Xaa 15 Glu Ile Leu Arg Gly Leu Xaa His Leu His Gln His Lys Val Ile His 30 Arg Xaa Ile Lys Gly Gln Asn Val Leu Leu Thr Glu Asn Ala Glu Val 45 50 Lys Leu Val Asp Phe Gly Xaa Xaa Ala Gln Leu Asp Arg Thr Val Gly 60 65 Arg Xaa Asn Thr Phe Ile Gly Thr Pro Tyr Trp Met Ala Pro Xaa Val 80 Ile Ala Cys Asp Glu Asn Pro Xaa Ala Thr Tyr Asp Phe Lys Xaa Asp 95 100 Leu Trp Ser Leu Gly Ile Thr Ala Ile Glu Met Ala Glu Gly Leu Pro 110 Leu Ser Val Thr Cys Thr Pro 125

<210> 504 <211> 140 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -14..-1

<400> 504

Met Phe Leu Thr Ala Leu Leu Trp Arg Gly Arg Ile Pro Gly Arg Gln -10 Trp Ile Gly Lys His Arg Arg Pro Arg Phe Val Ser Leu Arg Ala Lys 10 Gln Asn Met Ile Arg Arg Leu Glu Ile Glu Ala Glu Asn His Tyr Trp 25 Leu Ser Met Pro Tyr Met Thr Arg Glu Gln Glu Arg Gly His Ala Ala 40 Leu Arg Arg Glu Ala Phe Glu Ala Ile Lys Ala Ala Ala Thr Ser 60 Lys Phe Pro Pro His Arg Phe Ile Ala Asp Gln Leu Asp His Leu Asn 75 Xaa His Gln Glu Met Val Leu Ile Leu Ser Arg His Pro Trp Ile Leu 90 Trp Ile Thr Glu Leu Thr Ile Phe Thr Trp Ser Gly Leu Lys Asn Cys 105 Ser Leu Cys Glu Asn Glu Leu Trp Thr Ser Leu Tyr 120

<210> 505 <211> 59 <212> PRT <213> Homo sapiens

<220>

```
<221> SIGNAL <222> -14..-1
```

<400> 505

Met Ala Ala Leu Val Thr Val Leu Phe Thr Gly Val Arg Arg Leu His

-10

-5

Cys Ser Ala Xaa Leu Gly Arg Ala Ala Ser Gly Xaa Tyr Ser Arg Asn

5

Trp Leu Pro Thr Pro Pro Ala Thr Gly Pro Leu Pro Ser Ser Gln Thr

20

25

Gly His Mer Arg Met Ala Ala Leu Leu Pro Gln

Gly His Met Arg Met Ala Ala Leu Leu Pro Gln 35 40 45

<210> 506 <211> 101 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -36..-1

<400> 506

Met Gly Pro Tyr Asn Val Ala Val Pro Ser Asp Val Ser His Ala Arg -30 -25 -35 Phe Tyr Phe Leu Phe His Arg Pro Leu Arg Leu Leu Asn Leu Leu Ile -10 -15 Leu Ile Glu Gly Ser Val Val Phe Tyr Gln Leu Tyr Ser Leu Leu Arg Ser Glu Lys Trp Asn His Thr Leu Ser Met Ala Leu Ile Leu Phe Cys 15 20 Asn Tyr Tyr Val Leu Phe Lys Leu Leu Arg Asp Arg Xaa Xaa Leu Gly 35 40 Arg Ala Tyr Ser Tyr Pro Leu Asn Ser Tyr Glu Leu Lys Ala Asn Xaa 55 50

55

<210 > 507 <211 > 341 <212 > PRT <213 > Homo sapiens <220 >

Ala Ala Ser Xaa Gln

<221> SIGNAL <222> -55..-1

WO 99/31236 -354 - PCT/IB98/02122-

Phe Gln Arg Leu Asp Cys Ile Tyr Leu Asn Ala Gly Ile Met Pro Asn Pro Gln Leu Asn Ile Lys Ala Leu Phe Phe Gly Leu Phe Ser Arg Lys 50 Val Ile His Met Phe Ser Thr Ala Glu Gly Leu Leu Thr Gln Gly Asp 65 Lys Ile Thr Ala Asp Gly Leu Gln Glu Val Phe Glu Thr Asn Val Phe 80 Gly His Phe Ile Leu Ile Arg Glu Leu Glu Pro Leu Leu Cys His Ser 95 100 90 Asp Asn Pro Ser Gln Leu Ile Trp Thr Ser Ser Arg Ser Ala Arg Lys 110 115 Ser Asn Phe Ser Leu Glu Asp Phe Gln His Ser Lys Gly Lys Glu Pro 125 130 135 Tyr Ser Ser Ser Lys Tyr Ala Thr Asp Leu Leu Ser Val Ala Leu Asn 145 150 Arg Asn Phe Asn Gln Gln Gly Leu Tyr Ser Asn Val Ala Cys Pro Gly 160 Thr Ala Leu Thr Asn Leu Thr Tyr Gly Ile Leu Pro Pro Phe Ile Trp 180 175 Thr Leu Leu Met Pro Ala Ile Leu Leu Leu Arg Phe Phe Ala Asn Ala 195 190 Phe Thr Leu Thr Pro Tyr Asn Gly Thr Glu Ala Leu Val Trp Leu Phe 210 215 His Gln Lys Pro Glu Ser Leu Asn Pro Leu Ile Lys Tyr Leu Ser Ala 225 230 220 Thr Thr Gly Phe Gly Arg Asn Tyr Ile Met Thr Gln Lys Met Asp Leu 240 Asp Glu Asp Thr Ala Glu Lys Phe Tyr Gln Lys Leu Glu Leu Glu 255 260 Lys His Ile Arg Val Thr Ile Gln Lys Thr Asp Asn Gln Ala Arg Leu 275 270 Ser Gly Ser Cys Leu 285

```
<210> 508
<211> 108
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -42..-1
```

<400> 508 Met His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala - 30 Ile Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe -20 -15 Asp Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Ala Ile Ile 1 -5 Leu Gln Xaa Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser 15 10 Ala Ile Tyr Ala Ser Gln Thr Glu Gln Xaa Tyr Leu Lys Ile Xaa Lys 30 Gly Asp Gly Gly Ser Gly Ser Lys Gly Arg Pro Xaa Xaa Gln Thr Glu 45 50 Xaa Phe Leu Cys Ile Ser Lys Pro Ser Ser Phe Leu 60

```
<210> 509
<211> 80
<212> PRT .
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
<400> 509
Met Glu Glu Ile Ser Ser Pro Leu Val Glu Phe Val Lys Val Leu Cys
                       -20
                                            -15
Thr Asn Gln Val Leu Ile Thr Ala Arg Ala Val Pro Thr Lys Lys Ala
Ser Val Arg Cys Val Glu Lys Arg Phe Trp Ile Pro Lys Thr Thr Ser
        10
                               15
Lys His Leu Ser Arg Cys Ile Asp Gly Ile Ser Gly Phe Leu Asn Asp
                           30
Phe Thr Phe Cys Leu Glu Phe Ser Arg His Arg Cys Gln Leu Thr Glu
                       45
                                           50
<210> 510
<211> 158
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -44..-1
```

<400> 510 Met Ala Gly Phe Leu Asp Asn Phe Arg Trp Pro Glu Cys Glu Cys Ile -40 -35 Asp Trp Ser Glu Arg Arg Asn Ala Val Ala Ser Val Val Ala Gly Ile -25 -20 Leu Phe Phe Thr Gly Trp Trp Ile Met Ile Asp Ala Ala Val Val Tyr -10 -5 Pro Lys Pro Glu Gln Leu Asn His Ala Phe His Thr Cys Gly Val Phe 10 15 Ser Thr Leu Ala Phe Phe Met Ile Asn Ala Val Ser Asn Ala Gln Val 30 Arg Gly Asp Ser Tyr Glu Ser Gly Cys Leu Gly Arg Thr Gly Ala Arg 45 Val Trp Leu Phe Ile Gly Phe Met Leu Met Phe Gly Ser Leu Ile Ala 60 Ser Met Trp Ile Leu Phe Gly Ala Tyr Val Thr Gln Asn Thr Asp Val 75 Tyr Pro Gly Leu Ala Val Phe Phe Gln Asn Ala Leu Ile Phe Phe Ser 85 · 90 95 Thr Leu Ile Tyr Lys Phe Gly Arg Thr Glu Glu Leu Trp Thr 105

<210> 511 <211> 130 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -28..-1
```

<400> 511 Met Asn Trp Glu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu -25 -20 -15 Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu -10 - 5 Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu 10 15 Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu 25 30 Glu Leu Ala Tyr Gln Leu Ser Lyc Leu Gly Val Ser Leu Val Leu Ser 40 45 Ala Arg Arg .Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu 60 Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu 75 80 Thr Asp Thr Gly Ser His Glu Ser Gly Tyr Gln Ser Cys Ser Pro Gly

<220>
<221> SIGNAL
<222> -62..-1

## <400> 512

Ile Trp

Met Ser Gln Arg Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg -60 -55 Xaa Leu Ile Glu Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys -40 ~ 35 Val Leu Pro His Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val -30 -25 -20 Asn Ser Ile Leu Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys -5 -10 Ala Ser Lys His Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu 10 15 Leu Ala Thr Tyr Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro 25 Val Gln Ser Asn Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys 40 45 Thr Ile Gly Asn Asn Gly Asn Gln Ser His Lys Met Thr Thr Ser Arg 55 60 Cys Val Arg Leu Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val 70 75 Trp Ile Ser Glu Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr 90 95 Met Pro Thr Trp Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg 105 110 Ile Glu Asn Phe Lys Ser Gly Val Asp Ala Xaa Ser Ser Tyr Phe Lys 125 Ile Phe Lys Thr Lys His Asp 135

```
<210> 513
<211> 180
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 513
Met Asn Thr Val Leu Ser Arg Ala Asn Ser Leu Phe Ala Phe Ser Leu
                   -20
                                       -15
Ser Val Met Ala Ala Leu Thr Phe Gly Cys Phe Ile Xaa Thr Ala Phe
               - 5
Lys Asp Arg Ser Val Pro Val Arg Leu His Val Ser Arg Ile Met Leu
Lys Asn Val Glu Asp Phe Thr Gly Pro Arg Glu Arg Ser Asp Leu Gly
                       30
                                          3.5
Phe Ile Thr Phe Asp Ile Thr Ala Asp Leu Glu Asn Ile Phe Asp Trp
                    45
                                       50
Asn Val Lys Gln Leu Phe Leu Tyr Leu Ser Ala Glu Tyr Ser Thr Lys
               60
                                   65
Asn Asn Ala Leu Asn Gln Xaa Val Leu Trp Asp Lys Ile Val Leu Arg
                               80
Gly Asp Asn Pro Lys Leu Leu Lys Asp Met Lys Thr Lys Tyr Phe
                           95
Phe Phe Asp Asp Gly Asn Gly Leu Xaa Gly Asn Arg Asn Val Thr Leu
                       110
                                          115
Thr Leu Ser Trp Asn Val Val Pro Asn Ala Gly Ile Leu Pro Leu Val
                   125
                                       130
Thr Gly Ser Gly His Val Ser Val Pro Phe Pro Asp Thr Tyr Glu Ile
                                    145
Thr Lys Ser Tyr
           155
```

<210> 514 <211> 120 <212> PRT <213> Bos taurus

<400> 514

Met Met Thr Gly Arg Gln Gly Arg Ala Thr Phe Gln Phe Leu Pro Asp - 10 Glu Ala Arg Ser Leu Pro Pro Pro Lys Leu Thr Asp Pro Arg Leu Ala 20 25 Phe Val Gly Phe Leu Gly Tyr Cys Ser Gly Leu Ile Asp Asn Ala Ile 40 Arg Arg Arg Pro Val Leu Leu Ala Gly Leu His Arg Gln Leu Leu Tyr 55 Ile Thr Ser Phe Val Phe Val Gly Tyr Tyr Leu Leu Lys Arg Gln Asp 70 75、 Tyr Met Tyr Ala Val Arg Asp His Asp Met Phe Ser Tyr Ile Lys Ser 85 90 His Pro Glu Asp Phe Pro Glu Lys Asp Lys Lys Thr Tyr Gly Glu Val 100 105 Phe Glu Glu Phe His Pro Val Arg 115

```
<210> 515
<211> 1082
<212> DNA
<213> Homo sapiens
<400> 515
                                                                  60
gatcccagac ctcggcttgc agtagtgtta gactgaagat aaagtaagtg ctgtttgggc
taacaggate tectettgea gtetgeagee caggacgetg attecageag egeettaceg
cgcagcccga agattcacta tggtgaaaat cgccttcaat acccctaccg ccgtgcaaaa
ggaggaggeg eggeaagaeg tggaggeeet eetgageege aeggteagaa eteagataet
                                                                 240
gaccggcaag gagctccgag ttgccaccca ggaaaaagag ggctcctctg ggagatgtat
                                                                 300
                                                                 360
gettaetete ttaggeettt catteatett ggeaggaett attgttggtg gageetgeat
ttacaagtac ttcatgccca agagcaccat ttaccgtgga gagatgtgct tttttgattc
                                                                 420
tgaggatect geaaatteee ttegtggagg agageetaae tteetgeetg tgaetgagga
                                                                 480
qqctqacatt cgtqaggatq acaacattgc aatcattgat gtgcctgtcc ccagtttctc
                                                                 540
                                                                 600
tgatagtgac cctgcagcaa ttattcatga ctttgaaaag ggaatgactg cttac:tgga
cttqttgctg gggaactgct atctgatgcc cctcaatact tctattgtta tgcctccaaa
                                                                 660
aaatctggta gagetetttg geaaactgge gagtggeaga tatetgeete aaacttatgt
                                                                 720
                                                                 780
ggttcgagaa gacctagttg ctgtggagga aattcgtgat gttagtaacc ttggcatctt
tatttaccaa ctttgcaata acagaaagtc cttccgcctt cgtcgcagag acctcttgct
                                                                 840
                                                                 900
gggtttcaac aaacgtgcca ttgataaatg ctggaagatt agacacttcc ccaacgaatt
tattgttgag accaagatct gtcaagagta agaggcaaca gatagagtgt ccttggtaat
                                                                 960
aagaagtcag agatttacaa tatgacttta acattaaggt ttatgggata ctcaagatat
                                                                1020
                                                                1080
1082
aa
<210> 516
<211> 559
<212> DNA
<213> Homo sapiens
<400> 516
ctgctccagc gctgacgccg agccatggcg gacgaggagc ttgaggcgct gaggagacag
                                                                   60
                                                                  120
aggetggeeg agetgeagge caaacaeggg gateetggtg atgeggeeca acaggaagca
aagcacaggg aagcagaaat gagaaacagt atcttagccc aagttctgga tcagtcggcc
                                                                  180
                                                                  240
cgggccaggt taagtaactt agcacttgta aagcctgaaa aaactaaagc agtagagaat
                                                                  300
taccttatac agatggcaag atatggacaa ctaagtgaga aggtatcaga acaaggttta
atagaaatco ttaaaaaagt aagccaacaa acagaaaaga caacaacagt gaaattcaac
                                                                  360
agaagaaaag taatggactc tgatgaagat gacgattatt gaactacaag tgctcacaga
                                                                  420
ctagaactta acggaacaag tctaggacag aagttaagat ctgattattt actttgttta
                                                                  480
                                                                  540
559
aaaaaaaaa aaaaaaaa
<210> 517
<211> 110
<212> PRT
<213> Homo sapiens
<400> 517
Met Phe Cys Pro Leu Lys Leu Ile Leu Leu Pro Val Leu Leu Asp Tyr
                                   10
                                                     15
Ser Leu Gly Leu Asn Asp Leu Asn Val Ser Pro Pro Glu Leu Thr Val
                              25
His Val Gly Asp Ser Ala Leu Met Gly Cys Val Phe Gln Ser Thr Glu
                           40
```

<210> 518 <211> 4544 <212> DNA <213> Homo sapiens

<400> 518

```
ccgagaaggg cttcaggacg cgggaggcgc acttgcttca agtcgcgggc gtgggaacgg
                                                                      60
ggttgcaaaa cggggccttt ttatccgggc ttgcttccgg cgtcatggct caaagggcct
                                                                     120
tecegaatee tratgetgat tataacaaat eeetggeega aggetaettt gatgetgeeg
                                                                     180
ggaggetgae teetgagtte teacaaeget tgaccaataa gattegggag ettetteage
                                                                     240
aaatggagag aggcctgaaa tcagcagacc ctcgggatgg caccggttac actggctggg
                                                                     300
caggtattgc tgtgctttac ttacatcttt atgatgtatt tggggaccct gcctacctac
                                                                     360
agttagcaca tggctatgta aagcaaagtc tgaactgctt aaccaagcgc tccatcacct
                                                                     420
tectttgtgg ggatgeagge eccetggeag tggeegetgt getatateae aagatgaaca
                                                                     480
atgagaagca ggcagaagat tgcatcacac ggctaattca cctaaataag attgatcctc
                                                                     540
                                                                     600
atgctccaaa tgaaatgctc tatgggcgaa taggctacat ctatgctctt ctttttgtca
ataagaactt tggagtggaa aagattcctc aaagccatat tcagcagatt tgtgaaacaa
                                                                     660
                                                                     720
ttttaacctc tggagaaaac ctagctagga agagaaactt cacggcaaag tctccactga
tgtatgaatg gtaccaggaa tattatgtag.aggctgctca tggcctggct ggaatttatt
                                                                     780
                                                                     840
actacctgat geageceage etteaagtga gecaagggaa gttacatagt ttggtcaage
ccagtgtaga ctacgtctgc cagctgaaat tcccttctgg caattaccct ccatgtatag
                                                                     900
                                                                     960
gtgataatcg agatctgctt gtccattggt gccatggcgc ccctggggta atctacatgc
tcatccaggc ctataaggta ttcagagagg aaaagtatct ctgtgatgcc tatcagtgtg
                                                                    1020
ctgatgtgat ctggcaatat gggttgctga agaagggata tgggctgtgc cacggttctg
                                                                    1080
cagggaatgc ctatgccttc ctgacactct acaacctcac acaggacatg aagtacctgt
atagggcctg taagtttgct gaatggtgct tagagtatgg agaacatgga tgcagaacac
                                                                    1200
cagacacccc tttctctctc tttgaaggaa tggctggaac aatatatttc ctggctgacc
                                                                    1260
                                                                     1320
tgctagtccc cacaaaagcc aggttccctg catttgaact ctgaaaggat agcatgccac
ctgcaactca ctgcatgacc ctttctgtat attcaaaccc aagctaagtg cttccgttgc
                                                                     1380
tttccaagga aacaaagagt caaactgtgg acttgatttt gttagctttt ttcagaattt
                                                                     1440
                                                                     1500
atctttcatt cagttccctt ccattatcat ttacttttac ttagaagtat ccaaggaagt
cttttaactt taatttccat ttcttcctaa agggagagtg agtgatatgt acagtgtttt
                                                                     1560
                                                                     1620
gagattgtat acatatattc cagaacttgg aggaaatctt atttaagttt atgaatataa
                                                                     1680
ccatctgtta ctgttctaaa aatgtttaaa agaaactcaa tacagataaa gataaatatg
tgactattat tgggtattac acttcacttc tctttaatat ttttcctcca actggagggc
                                                                     1740
agacaatttt ctgacttgct tttctctagg tggttcattt tgaaagggga cagaaatata
                                                                     1800
actaaatgct tccaggagaa aaattccaag agttacaatc tggacttggt acctaaatat
                                                                     1860
                                                                     1920
cattttttaa attcttgatg cctatttgga ctagaggtaa acatactttc agattggcct
                                                                     1980
gtttttgtcg gtaaggcata cagcettcag aagccaacat ttttaatcaa aaacttataa
                                                                     2040
aacatgatga tcattgtgaa aattctgagt tgaaggttag tttaagataa gctaacaata
                                                                     2100
acagtotgtg ttttctctaa aataatotga gttttttgga actotttatt taaatatgtg
                                                                     2160
tgtttttcag tattcaaata agatcaggaa gccaattttc tatgtatgaa tatgctttaa
                                                                     2220
cctaggattt cagtccactc tgactgactt tctaaacttt aacttgggtt tttacagtga
                                                                     2280
ctatgcatta gtgctgactc tttggtataa gccataaaat attttccttc ctatcaattt
atotgaactt tggtotttto actaaattgt acagtattot acttotgttt aaaaagggga
                                                                     2340
gatgagaaag ggaatactat ctaaccaata acttgaacaa aaacactaaa ctaagcattt
                                                                     2400
                                                                     2460
aatagaaatg ctttttattg aggaggtatt atccagagtt catgcttaga acaaatgcat
ctttgcgtat cctagactta acaattcatc agtttctgag accacagaat caggttttcc
                                                                     2520
gtagtagata aagactetet ggtgetteaa attetgttea agtgttttga eteateaget
                                                                     2580
totactottt ctattactgc ctttgcctgg cttgttttgt ctctttgcaa ctgattttgc
                                                                     2640
aaaaaaaaat tgtagcttta aaataacagg gtctaagtat tttaaatgtg cctatttcac
                                                                     2700
```

```
agctctcttg gtcacaaaaa catgctattt ttattggaac ttcaaaccaa atccccactg
agtgtgtact ggttcctgca ggtagcagtc tcctattatc tcctgtttag caccaaaaga
                                                                     2820
gctaatatta ttggaaactg accttttaaa ggccactggc agtaggattt aaaaagcagc
                                                                     2880
ccactgetca gtttccagga tcagettect ccttetgtca ettgtgtaag ttggcactae
                                                                     2940
cttgtgcctc tcagattgct gaagtgctgc tggtaagcat gtgcatgctc tgcctttctt
                                                                     3000
gtgaaagttt tcaatcagcg atatcagcac ttacagtaag aagtaaaagt agtgcacagc
aaagctaatt tgcctttgcc tggggtgttc agcttgaaag aataaagctc atttggttta
                                                                     3120
gttaaatgtc ttactctact gtgcctatgc ttttagctgc gttactaagc aagggaaaaa
                                                                     3180
taacagtttc tctgagccag agaagacttg atcacagttc tccaagcatc gtgatagcaa
                                                                     3240
tgcttaaccc caggaagatt tcaaggcagg gagaagaaca tttcaaataa gattcttgtt
                                                                     3300
aacccattta tgcctagtgt tccattattg gaatgctaag cttgtgggag tcatttacat
                                                                     3360
cctactgctc aaagtcattg ccaaggtctg atttttcaca caaaaaattg caacccccag
                                                                     3420
cataaatggg ttagctactg tcatcagtta gcaaattcat ccacacaaac acaattagag
                                                                     3480
tttggttttt ttttaagett tteaaaaett aetaaaetgg cacaatttta tatgtatget
                                                                     3540
atttgttgta tttatgctta agagcaaaaa agttttgatg ggattttaaa ttcagcaaag
                                                                     3600
cctacaacgc tgagacaatc ccctaacaac atggtagtaa ctaaagaaac ttttatacta
                                                                     3660
ggcttcttag ttttaaaagg aagtggcatc attgtttcag ttctagtttg tatttttctc
                                                                     3720
tcagatattt ttcttcttta aaaatctttc ccagaagttg gttcctagaa aactcaatac
                                                                     3780
catcatctct tatctctata cagggactag gtaataaaac cttcaaaggt tgccaaaggt
                                                                     3840
catcaagcag tgttcattta tcctgtcaca tgtttctgtt tctatagtaa tttagaaatt
                                                                     3900
gcaaatagtt aacttttcat catgtaaaaa gttaacatta tcctatttcc atagatacca
                                                                     3960
tggacggcgg tgtggcctga gttgtcagtc tttaatcctg agtcatgtgg ctctcttttc
                                                                     4020
atctttgatg tcagttccaa ttatttggca tcaaaaacct tcatggtagg tagagtttta
                                                                     4080
ggtaaaagtg gatctagggt tactttcttt attaacattt cctaaataac tgaattgaga
                                                                     4140
gacatactet getactatgt ceteaggtta attititgtet gatettacga tgecetgeet
                                                                     4200
tttactaget actttagaaa tagaaaatgt gaagagtgae tatttacatg tatacteett
                                                                     4260
tggctgctag aactcatctg tagtccttta ttatttacac tgaattccaa tttcatttct
                                                                     4320
cttccgctaa gtaagagcac ctcattcctg tgttttctct actattgagc tgtagacgaa
                                                                     4380
ctgtttctct aattataaag caaactgttt gggatattca gggaaactac cccaatgtta
                                                                     4440
                                                                     4500
tgttgtcatt taatgggaaa ggctgggatc atatgtattt ctatgttctg taaagtattt
gacttactag ttctcaataa aattttatta ggactataaa aaaa
                                                                     4544
```

. **

<210> 519 <211> 1779 <212> DNA

<213> Mus musculus

<400> 519 ggtccggaat tcccgggtcg acccacgcgt ccgctggcct tgggcgcaga ccccggccgg 60 120 tecegggget geetetttaa gggagggggt ggageegega gteaggegeg aggageteea 180 gaaatettga ggccagagee cegeaceteg gegeageeat gagtgeggag gtgaaggtga 240 cagggcagaa ccaagagcag tttctgctcc ttgccaagtc ggctaagggg gcggcactgg ccacactcat ccaccaggtg ctggaggccc ctggtgtcta cgtgtttggg gaactgctgg 300 360 atatgcctaa tgttagagag ctggcagaaa gcgactttgc ctccaccttc cggctgctca cagtgtttgc ctatgggacc tatgcggact acttagctga agccaggaat ctcccccac 420 tgactgacgc acagaagaat aagcttcgac atctgtcagt tgtcactctg gctgccaaag 480 540 tcaagtgtat cccatatgca gtgttgctgg aggcccttgc ccttcgaaac gtgcgccagc 600 tggaagacct tgtgatcgag gctgtgtatg ctgatgtcct tcgtggctct ctggaccagc 660 gcaatcageg getagaggtt gattacagea tegggeggga catecagege caggacetea 720 gtgccatcgc ccagaccctg caagagtggt gcgtgggctg tgaggttgtg ttgtcgggca 780 tegaagagea ggteageegt gecaaceage acaaggagea geagetggge etgaageage 840 agatcgaaag tgaggttgcc aaccttaaga aaaccattaa agttacgaca gcagctgctg ctgcagccac ctcccaggat cctgagcaac acctgacaga gctgagagaa ccagcttctg 900 gcaccaacca gcgccagccc agcaagaaag cctccaaggg caagggactc cgagggagcg 960 ccaagatttg gtccaagtcg aactgaaagg acttgtttct tccctgggaa tgtggggtcc 1020 1080 cagetgeeta cetgeetace cettaggagt ceteagagee treetgtgee cetggecage 1140 tgataatgot agttcattac ttttcatctc ctccaccccc aagcataagc cacaccctct gtagggagga ggccagtgca ggtcatgttc tgttggtacc tcttatgtgt tccatgctct 1200 1260 tecceageae gettgetete ategtetete egeactgtgt etgeceatta eccetgteat tgagcaggtt ggcagtccta tggagggtgc tggctcttaa ccacccacac ctacccctgc

atgcctaatc	tgcagttcct	cctcctcccc	ttgcctagtg	ggctgcatct	gaaaagccat	1380
ggggaagggg	gtctccacct	tcattccagc	cttagagttc	tggagccagt	ctgctaccct	1440
gggagtcgct	ggacattttc	ctcccagaac	cccatcacac	tacaattgtt	tettteetet	1500
ctcatctcct	tgggcctggg	gatactgctg	cttcagtgac	cccagagcct	gagaacagct	1560
atttttgaga	tgttaagaaa	tggttctttg	ttgctcatca	tcttaggaag	cccaatggaa	1620
atcctggaag	gatttatatc	tcctcctgtg	gttctggtgg	ggaaggaaat	atagattgta	1680
tattaaaaat	aaaaaatata	tatgaatagg	tctatatata	ttgacacatg	acacagaaat	1740
aaatgtatga	gaaatgtatg	tacaaaaaa	aaaaaaaa			1779